

SCIENCE

12 December 1958

Volume 128, Number 333

Editorial	Ground Rules for Space Research 245	1479
Articles	The Significance of Vertebrate Metamorphosis: <i>G. Wald</i> 1481	
	A life cycle is circular; and its completion may involve two opposed metamorphoses, biochemical components of which pervade the vertebrate kingdom.	
	Hazard to Man of Carbon-14: <i>J. R. Totter, M. R. Zelle, H. Hollister</i> 1490	
	What problems are encountered in the quantitative estimation of the biological hazards of carbon-14?	
News of Science	De Hevesy to Receive \$75,000 Atoms for Peace Award; other events 1495	
Book Reviews	<i>Comparison of the Large-Scale Structures of the Galactic System with That of Other Stellar Systems</i> , reviewed by <i>H. Shapley</i> ; other reviews 1500	
Reports	Sexual Agglutination of Heterothallic Yeasts in Diverse Taxonomic Areas: <i>L. J. Wickerham</i> 1504	
	Hormonal Control of Onset of Corneal Reflex in the Frog: <i>J. J. Kollros</i> 1505	
	Factors Affecting the Relative Deposition of Strontium and Calcium in the Rat: <i>R. F. Palmer, R. C. Thompson, H. A. Kornberg</i> 1505	
	Phenylalanine Hydroxylation Cofactor in Phenylketonuria: <i>S. Kaufman</i> 1506	
	A Consideration of the Metabolic Rates of Some Shrew Tissues: <i>J. R. Redmond and J. N. Layne</i> 1508	
	Inhibition of Enzymatic Synthesis of Pantothenate by 2,3-Dichloroisobutyrate: <i>J. L. Hilton</i> 1509	
	Variability of Tooth Formation in Man: <i>S. M. Garn, A. B. Lewis, D. L. Polacheck</i> 1510	
	Formation of Metal Alkyls by Ionizing Radiation: <i>R. H. Johnsen and R. C. Gabler</i> 1510	
	Prolonged Natural Deferment of Hatching in Killifish: <i>R. W. Harrington, Jr., and J. S. Haeger</i> 1511	
Departments	Letters 1476	
	International Cancer Congress; Forthcoming Events; Equipment 1512	



New Foote Lithium Metal Dispersion . . . so reactive that it bursts into flame on contact with cold water. Light for the photo was supplied by the reaction.

NEW HIGH-REACTIVITY LITHIUM DISPERSIONS

Foote's new form of Lithium Dispersions realizes the high catalytic assets of lithium metal, lithium hydride, and lithium butyl . . . permitting faster, more complete, more controlled reactions.

AVAILABLE IN SEMI-COMMERCIAL QUANTITIES

Lithium Metal Dispersions:

bulk lithium dispersed in hydrocarbons.

Lithium Hydride Dispersions:

lithium dispersion hydrided in the dispersed state in hydrocarbons.

Lithium Butyl Solution:

prepared by the reaction of butyl chloride and lithium metal.
Available in various solvents, such as hexane and pentane.

No oxygen, please! Foote's new process prevents the formation of activity-reducing coatings. X-ray

analysis indicates that the surfaces of the dispersed metal are *clean* and *free* of hydroxide, carbonate, and oxide.

Small, uniform particle size makes the lithium metal and lithium hydride much more reactive than the usual forms. The small particle size facilitates reaction with the *whole* particle even if insoluble reaction products are formed. The uniform size means that *all* the metal will be used.

A more complete technical description of these new lithium dispersions is just off press. This literature and samples are available upon letterhead request to Technical Literature Department, Foote Mineral Company, 471 Eighteen West Cheltenham Building, Philadelphia 44, Pennsylvania.



FOOTE MINERAL COMPANY

Lithium Metal, Chemicals, Minerals • Strontium Chemicals • Welding Grade Ferro Alloys • Electrolytic Manganese Metal
Nickel • Steel Additives • Commercial Minerals and Ores • Zirconium, Titanium, Hafnium (Iodide Process) • Silicon Metal



SpectroPhotoFluorometer

reveals fluorescence in compounds
not previously known
to fluoresce . . .



Complete operating unit includes: A. Optical Unit; B. Photomultiplier Microphotometer; and C. Cathode-ray Oscillograph. If permanent record is desired, a Recorder (D) may be ordered separately (several models available).

4-8100 SpectroPhotoFluorometer, includes an optical unit, photomultiplier microphotometer, and a cathode-ray oscillograph, as illustrated above\$4200

4-8180 Recorder, Moseley, Model I, with required accessories, as illustrated.....\$1435

Samples as small as 0.1 ml. can be analyzed through use of a fused-quartz micro cell (Cat. No. 4-8114).

A Xenon Mercury Lamp (Cat. No. 5-8161) is available as an accessory item to produce higher sensitivity at activating wavelengths of the mercury line spectra.

Complete information in
Bulletin 2278—B
furnished upon request

Prior to the advent of this instrument, fluorescent measurement was limited to available filters ranging from 365 mμ up. Since many compounds are activated and fluoresce at wavelengths below 365 mμ, this factor severely limited various types of analysis. The new Aminco-Bowman SpectroPhotoFluorometer, with a range from 200 to 800 millimicrons, extends fluorescent measurement into the ultra-violet region. The instrument incorporates a Xenon Lamp in the optical unit, permitting excitation at wavelengths not previously possible. The Xenon continuum also permits scanning of the activation spectrum, a feature not previously possible with mercury lamp instruments.

Aminco will supply, upon request, reprints of technical papers discussing the fluorescent characteristics of the following compounds: Serotonin (Rep. 73, 74, 86); Lysergia Acid Diethylamide (LSD) (Rep. 72, 86); Reserpine (Rep. 72, 86); Tryptophan (Rep. 72, 86); Vitamins B⁶, B¹², (Rep. 86).

AMERICAN INSTRUMENT CO., INC.

8030 Georgia Ave., Silver Spring, Maryland

Letters

Human Rights and Society

Referring to C. W. Hartwig's comment [*Science* 128, 484 (1958)] on T. Dobzhansky's article "Evolution at work" [*Science* 127, 1091 (1958)], may I point out that the reference to my late colleague Whitehead is not precisely to the point.

Whitehead's remark that no society could survive if run on the principles of taking no thought for the morrow and no interest in the things that are Caesar's referred expressly to the responsibilities of individuals, not to their rights. The question whether it would be fatal to a practical social order if all men were equal in rights, and if no human being were used as means to an end, is an independent issue.

Hartwig's stricture on the "means to an end" formula is valid. All employment, all swapping of help, all "service," involves the use of human beings as means to an end. The formula is deadly without the one word that Kant used: "never as a means *only*." The word "only" makes the precise difference between employment and exploitation, and hence between industry and revolution. As to equality of rights, the phrase can run wild unless one specifies which ones among a long list of alleged rights are held "equal." Rights, strictly speaking, are not quantities; the claim of a right is either valid or invalid. And there is obviously no society in which all men have the same list of valid rights—the right to vote, for example. But it would not destroy society if all men had a right to life (barring murder), or an (equal) right to compete for (unequal) property. Properly defined, there is little difference between the "equal rights" proposition and the "never as means only" proposition. They both are demands, not scientific assertions—demands that a man be treated as a man, that is, as a self-governing organism. Acceptance of this demand, which is consistent with all the obvious inequalities in ability and disposition, including racial differentiations, and which requires no Bridgman anvil-apparatus to induce cooperation for social ends, could hardly be a peril to society.

WILLIAM ERNEST HOCKING
Madison, New Hampshire

Pavlov's Beliefs

This letter is offered as a footnote or postscript to the interesting paper "Pavlov and Lamarck" by Gregory Razran (1). In this paper Razran assembled the published evidence that shows that the

great Russian physiologist, I. P. Pavlov, believed that acquired characters were inherited and even believed that conditioned reflexes in mice could be transmitted from one generation to the next. The experiments that Pavlov conducted to prove this inheritance, however, were defective, and, as Razran shows, Pavlov withdrew all the claims that he had based on them (2, p. 385). After this unfortunate experience, Pavlov avoided the subject and omitted all references to it in his subsequent publications, even in those that, together, included all of his formal and informal addresses. Razran raises the important question as to whether Pavlov merely dropped the subject and directed his attention elsewhere or whether he actually abandoned his belief in the inheritance of acquired characters.

Apparently Pavlov never published anything that indicated he had definitely given up his belief that acquired characters were inherited. Razran was able to cite, however, two oral communications which are pertinent to Pavlov's reaction. One, quoted from W. Horsley Gantt, appears as follows: "Pavlov remarked to me that one of the biggest scientific errors of his life was his assertion that acquired habits could not be inherited." (Is there not a typographical error here? Should not the "not" be omitted?) The other is from Razran's own experience: "I asked him [Pavlov] specifically what his present views on the problem were. His answer was a shrug coupled with the sound of a typical Russian 'Ekh' which to me meant 'Don't ask' and I preferred not to pursue the question."

The oral answers thus are ambiguous and do not tell us whether Pavlov ever gave up his earlier belief. The following items do not remove the ambiguity completely, but they contribute to our knowledge of Pavlov's beliefs and give us some of the details of his unfortunate experience. First, Pavlov read a paper in 1917 before the Petrograd Biological Society entitled "The reflex of freedom" (3). In this he cited an incident from "The river of life," a story by Alexander Kuprin. Kuprin had described how a student had been conditioned by his earlier experiences until he had the mentality of a slave, but Pavlov went further. At this time he believed that conditioned reflexes in human beings were inherited (2, p. 286): "In Kuprin's story, 'The river of life,' there is described the suicide of a student who was tormented by his conscience after having betrayed his companions to the police. From a letter of the suicide, it was evident that he was the victim of the reflex of slavery inherited from his mother who was a priji-valka (upper class servant). If he had had an insight into his condition, he would first have understood his limitation, secondly he might, by systematic

measures, have developed control and successful suppression of this reflex."

The second item dates from 1929 and should be added to our oral tradition. It occurs in a footnote in *The Story of Evolution* by B. G. Gruenberg (4): "In an informal statement made at the time of the Thirteenth International Physiological Congress, Boston, August 1929, Pavlov explained that in checking up these experiments it was found that the apparent improvement in the ability to learn, on the part of successive generations of mice, was really due to an improvement in the ability to teach, on the part of the experimenter! And so this 'proof' of the transmission of modifications drops out of the picture, at least for the present." In this statement, Pavlov may have been covering up for an overzealous assistant.

The final item shows that Pavlov came as close as he could to disavowing his earlier belief in the inheritance of conditioned reflexes without stating specifically that he had done so. On 13 May 1927 he published his near-retraction in an article in *Pravda* (No. 106). This article was cited in a footnote to a paper, "Direct adaptation or natural selection," written by A. L. Takhtadzhian and published in the *Botanical Journal* (Moscow) in 1957 (5). It seems that Pavlov told his Russian colleagues precisely what he told the members of the 13th International Physiological Congress. In the footnote referred to, Takhtadzhian repeated almost word for word what Gruenberg had recorded from the Congress. He also quoted from Pavlov's 1927 paper in *Pravda* as follows: "The first experiments with hereditary transmission of conditioned reflexes of white mice have not yet been confirmed with improved methods and stricter control, so that I should not be numbered among those writers who affirm this transmission."

Pavlov, of course, was an honest scientist, but even here he does not say specifically that he disbelieves in the inheritance of acquired characters.

CONWAY ZIRKLE
Botanical Laboratories, University of
Pennsylvania, Philadelphia

References and Notes

1. G. Razran, "Pavlov and Lamarck," *Science* 128, 758 (1958).
2. I. P. Pavlov, *Conditioned Reflexes*, translated by C. V. Anrep (Oxford Univ. Press, London, 1927).
3. See "The reflex of freedom," in I. P. Pavlov, *Lectures on Conditioned Reflexes*, translated by W. Horsley Gantt (London, 1928), p. 286.
4. B. G. Gruenberg, *The Story of Evolution* (Garden City, New York, 1929), p. 327.
5. A. L. Takhtadzhian, "Direct adaptation or natural selection," *Botan. Zhur.* (1927), translated and published in English in *Current Digest of the Soviet Press* 9, No. 50, 9 (1958).

There is indeed a typographical error in the statement from Gantt quoted by Razran [see "Erratum," *Science* 128, 1076 (31 Oct. 1958)]—THE EDITORS.

Dr. Henry Hurwitz, Jr., Ph.D., Harvard (1941), is a former faculty member at Cornell University and was a theoretical physicist at the Los Alamos Scientific Laboratory during World War II. He joined General Electric in 1946, worked for ten years in the field of fission power at the Knolls Atomic Power Laboratory, and now serves as manager of the *Nucleonics and Radiation Section* at the General Electric Research Laboratory.



Forward toward fusion

General Electric's Dr. Henry Hurwitz, Jr., leads a long-range program in thermonuclear research

Achieving a controlled thermonuclear reaction—fusion power—is one of the most exciting challenges in modern science, but it is also a problem whose practical solution seems decades away. Even though the final payoff may be far in the future, General Electric believes the goal of an unlimited source of energy is so important to man's future that a substantial research effort in fusion is justified *now*.

At the General Electric Research Laboratory, Dr. Henry Hurwitz, Jr., is leading a group of scientists who are giving their undivided attention to the problems of achieving and holding the fantastic temperatures—in the range of 100 million degrees—required to sustain a thermonuclear reaction. Using

large and complex research equipment which they have designed, Dr. Hurwitz and his associates are exploring the properties of plasma and the physics of magnetic containment.

General Electric's fusion program is another example of a long-range research effort in which scientists are being provided the tools, the incentives, and the freedom to seek progress through the acquisition of new scientific knowledge.

Progress Is Our Most Important Product

GENERAL  ELECTRIC



Leonardo da Vinci...on experiments

"I shall begin by making some experiments before I proceed any further; for it is my intention first to consult experience and then show by reasoning why that experience was bound to turn out as it did. This, in fact, is the true rule by which the student of natural effects must proceed: although nature starts from reason and ends with experience, it is necessary for us to proceed the other way around, that is — as I said above — begin with experience and with its help seek the reason.

Experience never errs; what alone may err is our judgment, which predicts effects that cannot be produced in our experiments. Given a cause, what follows will of necessity be its true effect, unless some external obstacle intervenes. When that happens, the effect that would have resulted from the cause will reflect the nature of the obstacle in the same proportion as the obstacle is more or less powerful than the cause."

—Notebooks, circa 1500

THE RAND CORPORATION, SANTA MONICA, CALIFORNIA
A nonprofit organization engaged in research on problems related to national security and the public interest

WALLA
PAUL
LAURE
PAUL
GEORGE
CHAUD
MARCO
THOM
MINA
WILLI
ALAN
PAUL
DAEL

DONAL
KONKA
EDWIN

SARAH
HAMIL
WOLF
E. M
SCHNE
WOLSA

ENR

SCI
SCIEN
day by
ment
The j
format
at sec
1879,
to Per
Edit
ence
Massa
Manus
and su
respon
the of
tailed
scripts
125, 16

Disp
address
St., Ne
Char
1315 M
4 week
stencil
both o
bers, if

Ann
\$1.50;
Cable

AMERICAN ASSOCIATION
FOR THE
ADVANCEMENT OF SCIENCE

Board of Directors

WALLACE R. BRODE, *President*
PAUL E. KLOPSTED, *President Elect*
LAURENCE H. SNYDER, *Retiring President*
PAUL M. GROSS
GEORGE R. HARRISON
CHAUNCEY D. LEAKE
MARGARET MEAD
THOMAS PARK
MINA REES
WILLIAM W. RUBEY
ALAN T. WATERMAN
PAUL A. SCHERER, *Treasurer*
DAEL WOLFE, *Executive Officer*

DAEL WOLFE, *Executive Officer*
GRAHAM DUSHANE, *Editor*
JOSEPH TURNER, *Assistant Editor*
ROBERT V. ORMES, *Assistant Editor*

Editorial Board

DONALD J. HUGHES H. BURR STEINBACH
KONRAD B. KRAUSKOPF WILLIAM L. STRAUS, JR.
EDWIN M. LERNER EDWARD L. TATUM

Editorial Staff

SARAH S. DEES, LUCILLE GUINARD, NANCY S.
HAMILTON, WILLIAM HASKELL, OLIVER W. HEAT-
WOLF, YUKIE KOZAI, JUDITH B. LEVIN, ELLEN
E. MURPHY, BETHSABE PEDERSEN, MADELINE
SCHNEIDER, NANCY L. TEIMOURIAN, MARIA A.
WOLSAK.

EMIL J. SCHERAGO, *Advertising Representative*

SCIENCE, which is now combined with THE SCIENTIFIC MONTHLY, is published each Friday by the American Association for the Advancement of Science at Business Press, Lancaster, Pa. The joint journal is published in the SCIENCE format. Entered at the Lancaster, Pa., Post Office as second class matter under the Act of 3 March 1879. SCIENCE is indexed in the *Reader's Guide to Periodical Literature*.

Editorial and personnel-placement correspondence should be addressed to SCIENCE, 1515 Massachusetts Ave., NW, Washington 5, D.C. Manuscripts should be typed with double spacing and submitted in duplicate. The AAAS assumes no responsibility for the safety of manuscripts or for the opinions expressed by contributors. For detailed suggestions on the preparation of manuscripts, book reviews, and illustrations, see *Science* 125, 16 (4 Jan. 1957).

Display-advertising correspondence should be addressed to SCIENCE, Room 740, 11 West 42 St., New York 36, N.Y.

Change of address notification should be sent to 1515 Massachusetts Ave., NW, Washington 5, D.C. 4 weeks in advance. If possible, furnish an address stencil label from a recent issue. Be sure to give both old and new addresses, including zone numbers, if any.

Annual subscriptions: \$8.50; foreign postage, \$1.50; Canadian postage, 75¢. Single copies, 35¢. Cable address: Advancesci, Washington.



Ground Rules for Space Research

The newly formed National Aeronautics and Space Administration is now seeking in its organizational set-up the way of wisdom between two extremes. On the one side is the extreme of no central organization, which could mean that all participating laboratories find themselves conducting variants of the same experiment; on the other side is the extreme of complete organization, which could mean that the effort to discover the best way to conduct a given experiment results in very few experiments getting underway. Where lies the golden mean?

The new agency was established by Congress as part of the answer to criticisms of research and development as previously conducted by the armed services. According to critics, the armed services together with the Department of Defense produced a set-up that managed the singular feat of erring in both directions at once. Competition among the Army, Navy, and Air Force resulted in wasteful duplication, while the Defense Department's efforts to control duplication resulted in costly delays.

To avoid some of the shortcomings of earlier programs, the Space Administration appears to be planning to conduct a strong research program within its own facilities—this in addition to directing through outside contracts a broad range of efforts by research groups in universities and industry. Besides giving it the advantage of being able to initiate its own projects, a strong house program will enable the agency to give more effective direction to its outside research. To direct outside research, the Space Administration should have a staff of talented scientists upon whom, in conjunction with its special advisory committees, it can call for advice. Scientists being what they are, the opportunity for creative work that a house program affords would bring to the agency men of a higher caliber than it would otherwise be able to obtain.

Since the major strength of the earlier efforts in space research lay in the armed service programs, the new agency will look to this source both for individual scientists and for working groups. Opposition by the armed services is strong, and the services feel the most justified in those areas in which they have been the most farsighted. So far the new agency has had mixed success. One large transfer of personnel to the Space Administration was a group of approximately 150 scientists who had been engaged in the Vanguard program of the Naval Research Laboratory. A second transfer was the Army's Jet Propulsion Laboratory at Pasadena, California, which is operated by California Institute of Technology. However, the Space Administration also wanted to acquire the Army Ballistic Missile Agency at Huntsville, Alabama, with its staff of 2000 scientists under Wernher von Braun, but President Eisenhower has permitted the Army to keep control.

Detailed plans for the organization of research in the Space Administration have yet to be completed, and it would seem that the form they finally take will depend in part upon further developments outside the agency. The over-all problem is whether the earlier dispute over what properly belongs to the Army, Navy, and Air Force will now be replaced by the dispute over what is properly military and what civilian. The hope is that in place of rivalry we shall, with these new protagonists, now find cooperation.—J.T.

MECHANIZED ORACLE EXPLORES BELL SYSTEM COMMUNICATIONS



At monitoring console, designer H.D. Irvin watches performance of "Sibyl" during test of user-reaction to experimental telephones. A computer-like machine, Sibyl simulates the functions of future communications devices and records interplay between phones and users. Sibyl is named after the women oracles of ancient Greece.

A mechanized "oracle" is helping Bell Telephone Laboratories predict the future in communications devices and systems.

The oracle is "Sibyl," a computer-like machine developed by Bell Laboratories engineers and psychologists. It can simulate the action of many kinds of communications devices. Through Sibyl, new kinds of telephone service can be evaluated without the considerable expense of building actual equipment. Observing and recording users' reactions to the simulated equipment, Sibyl provides indications of how users would react to proposed new systems features and equipment.

Sibyl, for example, is used to test the reaction of Bell Laboratories people to experimental push-button telephones. Each test subject has a push-button telephone in his office and he uses it in the ordinary course of his busi-

ness. But the set is not connected directly to the local PBX: it is connected *through* Sibyl, which performs the special signaling functions required by such a push-button telephone. In this way, push-button telephone service is given to a group of people without modifying the PBX, or providing completely instrumented push-button telephones.

At the same time, Sibyl gathers information on how the call was placed—date, time, originator, speed of operation, errors, whether the line was busy or the call completed. Sibyl does all this without violating the privacy of telephone conversations.

Bell engineers expect that Sibyl will provide a better understanding of the relationship between telephone equipment and the people who use it. Sibyl's rapid and economical technique for evaluating new types of telephone sets is an important contribution to the art of telephony.



BELL TELEPHONE LABORATORIES

WORLD CENTER OF COMMUNICATIONS RESEARCH AND DEVELOPMENT

The Significance of Vertebrate Metamorphosis

A life cycle is circular; and its completion may involve two opposed metamorphoses, biochemical components of which pervade the vertebrate kingdom.

George Wald

"Nicodemus saith unto him, How can a man be born when he is old? can he enter the second time into his mother's womb, and be born?"

"Jesus answered, Verily, verily, I say unto thee, Except a man be born of water . . ."—John, 3: 4, 5.

One of Thomas Mann's novels begins with the words, "Very deep is the well of the past." This is the well from which all biology is drawn. Physics and chemistry deal with what is; biology with what has become. In biology one is never far from history; and each living organism carries fragments of this history with it, as vestiges and recapitulations, anatomical and, as we shall see, biochemical.

I was led into this subject through the study of visual systems. I shall begin with them since they still provide the main thread of the argument, though by now it branches widely.

What we are concerned with here is an aspect of biology at the molecular level. Like all such developments, it runs closely parallel with earlier arguments based primarily upon anatomy. This is hardly surprising, for the anatomy of an organism is the greatly magnified expression of its chemistry; and the short- and long-term changes in anatomy that con-

stitute the organism's embryogeny and evolution, by the same token, express chemical changes. The biochemist is a biologist whose dissections have reached the molecular level. Far from removing him from biology, this gives him new opportunities to pursue it.

For like reasons, some of the viewpoints and conclusions expressed here (1) were reached long ago by other paths. They will bear this reiteration and the new support that biochemistry brings them.

Primacy of the Spawning Environment

Two kinds of visual system are found in the rods of vertebrate retinas. One is based upon the red visual pigment, rhodopsin, formed by the combination of the protein opsin with retinene, the aldehyde of vitamin A. The other is based upon the purple pigment, porphyropsin, formed from the same type of opsin combined with retinene₂, the aldehyde of vitamin A₂. Retinene₂ and vitamin A₂ differ from retinene and vitamin A only in possessing an added double bond in the ring (Fig. 1) (see 2).

The porphyropsin system was first discovered in fresh-water fishes. Marine fishes and land vertebrates characteristically possess the rhodopsin system (3, 4) (Figs. 2 and 3).

What of the fishes that are neither fresh-water nor marine, but migrate between both environments? It would be well before discussing them to clarify somewhat their biological position.

Most fishes are restricted throughout their lives to narrow ranges of salinity. Such forms are called "stenohaline" and are of two kinds, fresh-water and marine. A much smaller group of fishes can live as adults in a wide range of salinities. They are called "euryhaline," and, again, are of two kinds, anadromous and catadromous, meaning "upstream" and "downstream." These terms refer to the direction of the spawning migrations. Salmon, for example, are typically anadromous forms, coming upstream to spawn, whereas the "fresh-water" eels are catadromous, going downstream to the sea on their spawning migration.

It is probably true, however, that no euryhaline fish has to leave its spawning environment to complete a normal life cycle. Many instances are known in which anadromous fishes remain permanently in fresh water. The same is true of such an anadromous cyclostome

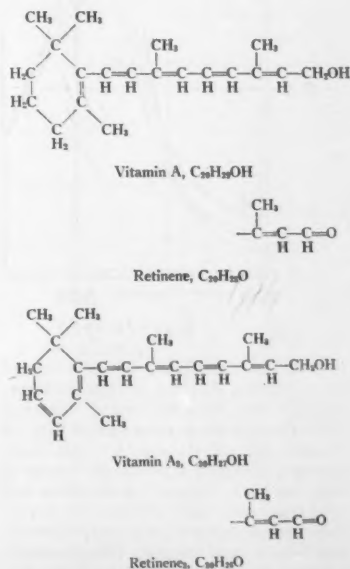


Fig. 1. Structures of vitamin A, retinene, vitamin A₂, and retinene₂.

The author is professor of biology in the Biological Laboratories of Harvard University, Cambridge, Mass.

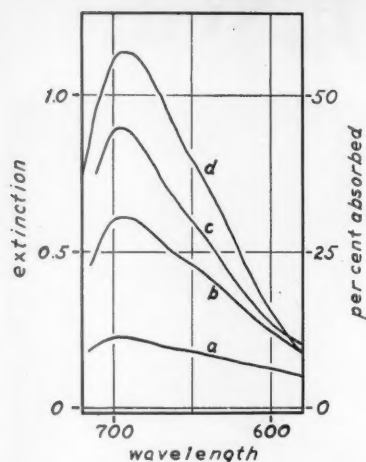


Fig. 2. The vitamin A_2 of the retinas of fresh-water fishes. Antimony chloride tests with extracts of wholly bleached retinas display only the absorption band maximal at 690 to 696 $m\mu$ characteristic of vitamin A_2 . This result has been obtained invariably in about 12 widely distributed species of fresh-water teleost. In almost all cases the visual pigment has also been extracted and this pigment has been found to be porphyropsin, with λ_{max} about 522 $m\mu$. [From Wald (3)]

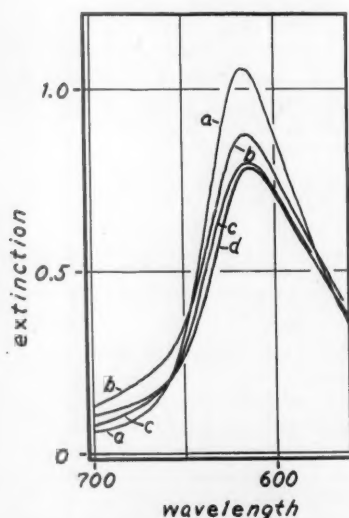


Fig. 3. The vitamin A_1 of the retinas of marine fishes. Spectra of the antimony chloride tests with extracts of bleached retinas reveal the λ_{max} at 615 to 620 $m\mu$ characteristic of vitamin A_1 . This result has been obtained with a great variety of bony, and a few elasmobranch, fishes and is characteristic also of land vertebrates. Two wrasse fishes (*Labridae*), however, the cunner and tautog, though wholly marine, are exceptional in having a predominance of vitamin A_2 in their retinas. [From Wald (3)]

as the sea lamprey, which has recently colonized the Great Lakes and virtually destroyed the fresh-water fisheries there.

So far as we know, the spawning environment is always fixed. The eggs, the sperms, or the embryos, perhaps sometimes all three, are stenohaline. Euryhalinity develops later in life and permits, though does not compel, these animals to migrate to the other environment. Migration is only a potentiality, which some of these forms exploit regularly and others rarely. The salmonids are essentially fresh-water fishes with the privilege of going to sea as adults; the fresh-water eels are marine fishes with the capacity of coming as adults into fresh water.

The significant biological statement concerning such fishes is not that they migrate but that, being fixed in spawning environment, they are euryhaline as adults. I should like on this basis to redefine the terms applied to them. An anadromous fish is a euryhaline form which spawns in fresh water; a catadromous fish, one which spawns in the sea (3).

On examining the visual systems of several genera of salmon, I found that all of them possess mixtures of the rhodopsin and porphyropsin systems, yet primarily the latter, characteristic of the spawning environment. Conversely, the American fresh-water eel possesses a mixture of both visual pigments, in which rhodopsin—again the spawning type—predominates (Fig. 4) (5). Certain other anadromous fishes—alewife, white perch—possess porphyropsin almost alone (Fig. 5). All the euryhaline fishes examined follow a simple rule: all of them possess, either predominantly or exclusively, the type of visual system characteristically associated with the spawning environment (3, 6).

To a first approximation these patterns are genetic and independent of the immediate environment. The salmonids which were found to possess mixtures of both visual systems had spent their entire lives in fresh water. Alewives just in from the sea on their spawning migration possess porphyropsin almost exclusively. Most striking of all, the cunner and tautog, members of the wholly marine family of *Labridae*, the wrasse fishes, possess porphyropsin; this is the only type of marine fish yet known to do so (3, 6).

Since the distribution of visual systems among fishes is genetic, one may ask whether it fits into some evolutionary

pattern. Many paleontologists are convinced that the vertebrate stock originated in fresh water. It is from such fresh-water ancestors that our fresh-water fishes were ultimately derived (7). The observation that these animals characteristically have the porphyropsin system suggests that this may have been the ancestral vertebrate type. Subsequently vertebrates undertook two great evolutionary migrations, one into the sea, the other to land. Both led them to the use of rhodopsin in rod vision, for this is the pigment we find characteristically in marine fishes and land vertebrates. The euryhaline fishes are intermediate between fresh-water and marine forms both in life history and in the composition of their visual systems. In this regard one can arrange the fishes in such an ordered sequence as that shown in Fig. 6.

Euryhaline Fishes and Amphibia

One can hardly develop such an argument as outlined above without raising questions regarding the amphibia. These

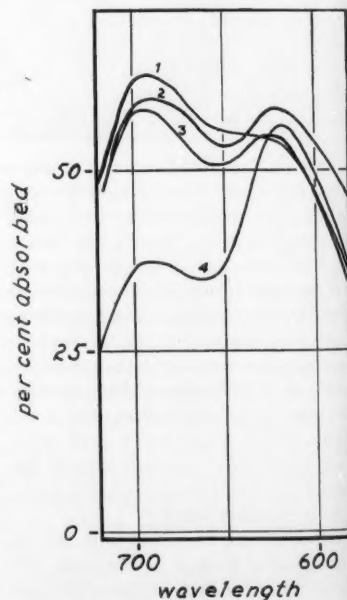


Fig. 4. Retinal vitamins A in euryhaline fishes. Spectra of antimony chloride tests with extracts of bleached retinas from (1) chinook salmon, (2) rainbow trout, (3) brook trout, and (4) the American "fresh-water" eel. All these tissues contain both vitamins A_1 and A_2 , the anadromous salmonids a predominance of vitamin A_2 , the catadromous eel a higher proportion of vitamin A_1 . [From Wald (3)]

animals come between fresh-water fishes and land vertebrates, just as the euryhaline fishes do between fresh-water and marine fishes. Most amphibia, like most euryhaline fishes, spawn in fresh water. Indeed, the life cycle of the common frog runs strikingly parallel with that of such an anadromous fish as the salmon. Both originate and go through a larval period in fresh water. Both, after undergoing deep-seated anatomical and physiological changes which can in both be described as metamorphosis, migrate for the growth phase, the salmon to sea, the frog to land. Both return to fresh water at sexual maturity to spawn. What land is to the frog, the sea is to the salmon. *The euryhaline fishes are the amphibia among the fishes.*

In this sense one might speak of almost all amphibia as "anadromous," meaning that they spawn in fresh water and are free, as adults, to go back and forth between fresh water and the land. [One would like to commit further etymological atrocities. The essence of the euryhaline condition is the capacity to migrate, not so much between low and high salt concentrations as between hydrating (fresh-water) and dehydrating (sea and land) conditions. In this sense the amphibia are "euryhaline." Obviously one needs new terms, firmly grounded in ecological essentials rather than in trivialities.] A few amphibia (red-backed and tree salamanders) have developed special devices for living permanently ashore. I know of no "catadromous" amphibian—that is, one that spawns on land and goes through its growth phase in the water. A number of aquatic reptiles, however (alligators, fresh-water snakes, and turtles), fulfill this description nicely.

If these are substantial parallels, and if the spawning environment decides the pattern of visual pigments, then one should expect such an "anadromous" amphibian as the common frog to possess mainly porphyropsin, like a salmon. Yet rhodopsin was originally discovered in the rods of frogs, and for a long period all that we knew of this pigment was learned with frogs.

In this dilemma I turned to a tailed amphibian, with the thought that it might display more primitive properties than the tail-less types. Adults of the common New England spotted newt were found to possess porphyropsin exclusively (8, p. 337). This brought a first amphibian into the same fold with certain anadromous fishes but left the frog

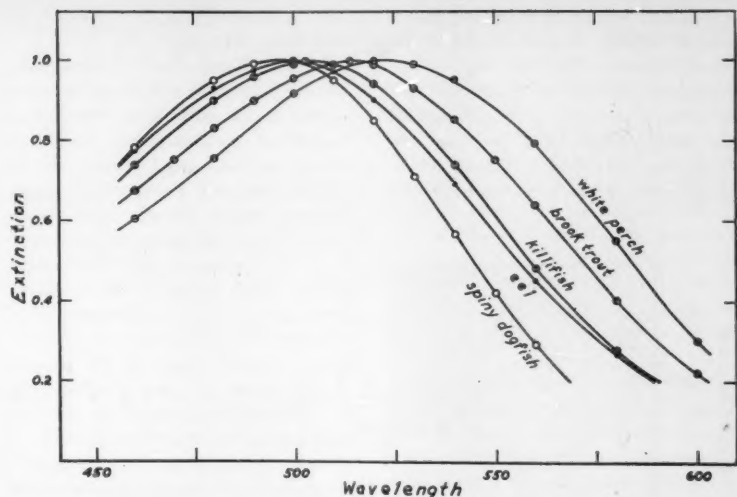


Fig. 5. Spectra of the visual pigments of various fishes, illustrating the transition from an exclusively rhodopsin to an exclusively porphyropsin system, correlated with salinity relations. The permanently marine dogfish possesses rhodopsin alone (λ_{max} about 497 mμ); the catadromous eel and brackish-water killifish, predominantly rhodopsin; the anadromous brook trout, predominantly porphyropsin; and the anadromous white perch, wholly porphyropsin (λ_{max} about 522 mμ). [From Wald (6)]

in a more aberrant position than ever.

On examining bullfrogs in metamorphosis, however, I found that tadpoles just entering the metamorphic crisis possess porphyropsin almost entirely, whereas newly emerged frogs have changed almost entirely to rhodopsin (9). The anatomical metamorphosis, which in this species takes about three weeks, is accompanied by this biochemical metamorphosis of visual systems. The bullfrog enters metamorphosis with porphyropsin, like a fresh-water fish, and emerges with rhodopsin, like a land vertebrate (10) (Fig. 7).

Individual amphibia, therefore, like euryhaline fishes, may display both types of visual system. It seemed for a time that one difference between both groups might be that in euryhaline fishes the patterns of visual system are fixed, whereas in amphibia they change abruptly with metamorphosis. I shall have more to say of this later.

Biochemistry of Metamorphosis

At the time the metamorphosis of visual systems was discovered in the bullfrog, another such change in the same species had already been described. McCutcheon (11) had found that the properties of hemoglobin in this animal change markedly at metamorphosis. The

oxygen equilibrium curve of hemoglobin, measured at one temperature and pH, goes through a remarkable transition between tadpoles and adults. The hemoglobin of tadpoles has a high affinity for oxygen, and it seemed from McCutcheon's measurements that the shape of its oxygen equilibrium curve might be hyperbolic, whereas the hemoglobin of young adults has a relatively low affinity for oxygen, and its equilibrium curve is distinctly S-shaped.

Riggs (12) reexamined this situation

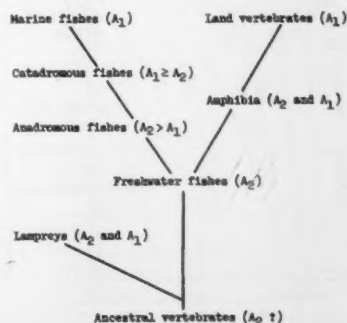


Fig. 6. Distribution of vitamins A_1 and A_2 in vertebrate retinas. The observations, all made on contemporary animals, are here correlated with the present ecology. They may also, however, represent evolutionary sequences, and in that case they convey the suggestion that primitive vertebrate vision was based upon vitamin A_2 .

in our laboratory. He confirmed McCutcheon's finding of a striking loss of oxygen affinity at metamorphosis. He found, however, that the shape of the oxygen equilibrium curve does not alter at metamorphosis; it is equally sigmoid throughout development. He found another important change: tadpole hemoglobin exhibits almost no loss of oxygen

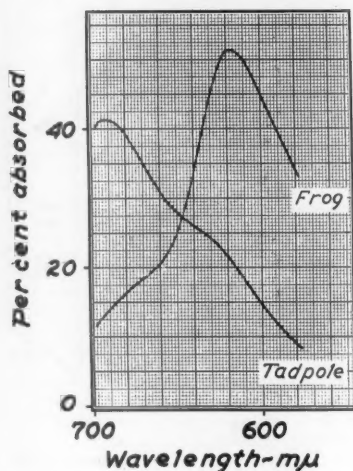


Fig. 7. Biochemical metamorphosis of visual systems in the bullfrog, *Rana catesbiana*. The tadpole just entering the metamorphic crisis has in its retina vitamin A_2 (that is, porphyropsin) with only a trace of vitamin A_1 and rhodopsin, whereas the newly emerged froglet has just the reverse pattern. [From Wald (9)]

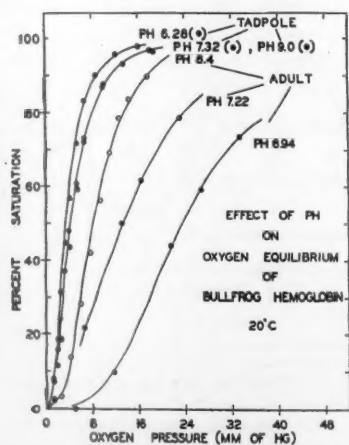


Fig. 8. Biochemical metamorphosis of hemoglobin in the bullfrog, *Rana catesbiana*. Tadpole hemoglobin has a high affinity for oxygen and virtually no loss of affinity on acidification (the Bohr effect); adult hemoglobin has a much lower affinity for oxygen and a large Bohr effect. [From Riggs (12)]

affinity on acidification (that is, no Bohr effect), whereas frog hemoglobin has a very large Bohr effect (Fig. 8).

It is clear therefore that hemoglobin, like the pigment of rod vision, metamorphoses in the bullfrog at the time of anatomical metamorphosis. Both substances are conjugated proteins. In the rod pigment, it is the prosthetic group, retinene, which changes; the protein opsin, so far as known, remains unaltered. In hemoglobin it is the protein, globin, which changes; the prosthetic group, heme, is the same always (13).

Recently Frieden *et al.* (14) have described a third change in the proteins of this species at metamorphosis (Fig. 9). In the bullfrog tadpole the predominant proteins of the blood plasma are globulins. At metamorphosis, the protein concentration of the plasma doubles, and albumins become predominant. These changes can be induced prematurely, just as can anatomical metamorphosis, by administering triiodothyronine.

Still another type of biochemical change has been shown to accompany metamorphosis in frogs and salamanders. Fishes excrete most of their nitrogen as ammonia, whereas land vertebrates excrete their nitrogen primarily as urea or uric acid. Munro (15) showed some years ago that whereas the tadpoles of the frog, *Rana temporaria*, excrete the great bulk of their nitrogen as ammonia, at the metamorphic crisis this animal goes over to excreting its nitrogen primarily as urea (Fig. 10). At this time, also, arginase, the last in the chain of enzymes that forms urea, makes its first appearance in the liver. Recently Munro (16) has demonstrated similar changes accompanying metamorphosis in the toad *Bufo bufo*, the salamanders *Triturus vulgaris* and *T. cristatus*, and the axolotl *Siredon mexicanum*.

These observations make a beginning with the biochemistry of metamorphosis. They show that just as animals in metamorphosis undergo radical alterations in anatomy, so their biochemistry is fundamentally revised at the same time. Indeed both kinds of change, anatomical and biochemical, herald an ecological transition, for they are followed by radical changes of habitat. They mark also an evolutionary transition, for these changes offer the most striking instances we know of recapitulation. The amphibian in metamorphosis seems to repeat in rapid summary the changes which accompanied the emergence of vertebrates from fresh water onto land. The transformation of visual systems and of the

pattern of nitrogen excretion seems to provide clear instances of *biochemical recapitulation*. The changes in hemoglobin also seem to involve aspects of recapitulation (8, p. 337; 17). Whether the changes in serum proteins have this character, it is too early to say. In any case, in metamorphosis the anatomy, the biochemistry, and, shortly afterward, the ecology all are transformed, and frequently in some degree of accord with the animal's evolutionary history.

It is interesting to realize how closely these patterns hold together. An aberration in one of them seems to call forth appropriate aberrations in the others. The mud puppy, *Necturus maculosus*, for example, remains to some degree a permanent larva, never losing its external gills and never emerging from the water. Some years ago I found that adult mud puppies have porphyropsin alone, like a fresh-water fish (8).

The clawed toad, *Xenopus laevis*, a

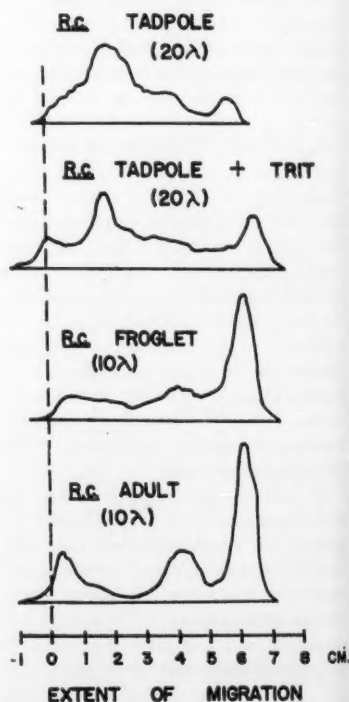


Fig. 9. Biochemical metamorphosis of plasma proteins in the blood of the bullfrog, *Rana catesbiana*. Tadpole plasma contains a predominance of globulins that migrate slowly on electrophoresis at pH 8.6; in the froglet a change to a predominance of rapidly migrating albumin takes place. This change is also induced prematurely by treatment of tadpoles with triiodothyronine (Trit). The volume of serum used is indicated in parentheses. [From Frieden, Herner, Fish, and Lewis (14)]

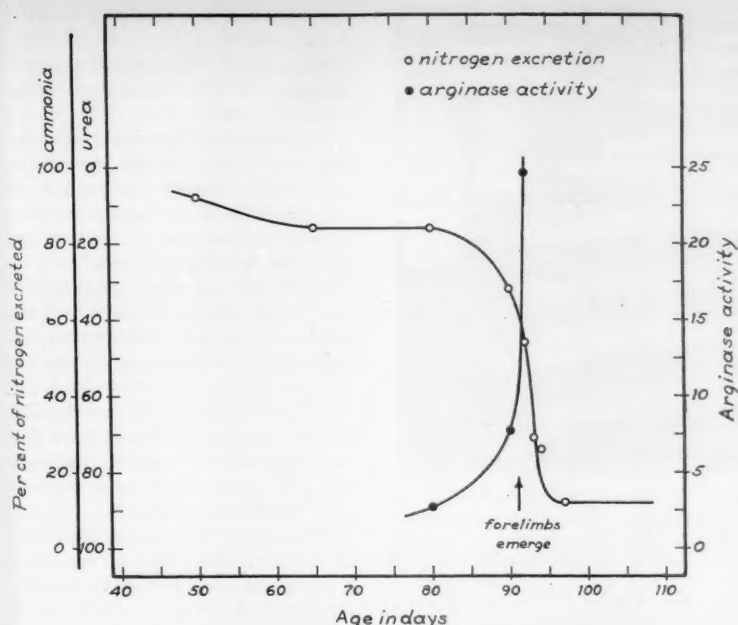


Fig. 10. Biochemical metamorphosis of nitrogen excretion in the European frog, *Rana temporaria*. At the metamorphic crisis, this animal changes from excreting about 90 percent of its nitrogen as ammonia to excreting about 90 percent as urea. Simultaneously, the activity of arginase, the enzyme that hydrolyzes arginine to form urea, rises sharply in the liver. [From Wald (8), drawn from the data of Munro (15)]

member of the peculiar family Aglossa, which possesses neither tongue nor teeth, is a purely aquatic form, which, though it metamorphoses, ordinarily never emerges from the water. Adults of this species possess, in their retinas, vitamin A₂ and porphyropsin almost exclusively (18). Underhay and Baldwin (19) have recently shown that this species also exhibits peculiar changes in the pattern of its nitrogen excretion. As a tadpole it excretes nitrogen primarily as ammonia. At metamorphosis, like other amphibia, it begins to change over toward urea excretion, so that at the height of metamorphosis it excretes a little more nitrogen as urea than as ammonia. Toward the end of metamorphosis, however, it swings back again, so that the adult excretes about three times as much ammonia as urea nitrogen. It is as though this animal, having got ready to leave the water, changed its mind; and both the getting ready and the change of mind are reflected in the nitrogen excretion. Indeed, *Xenopus* can change its mind again; for if kept moist while yet out of water it accumulates huge amounts of urea, perhaps as a device for conserving water such as is practised by the elasmobranch fishes. Its return to water is attended by a massive excretion of urea

accompanied by very little ammonia (20).

We see, therefore, that even the aberrations of amphibian metamorphosis, anatomical and ecological, are paralleled closely by the biochemistry. It is probably true that in all cases in which the anatomy or the ecology changes, the biochemistry also changes. Indeed the biochemistry may have a primary status; the visible alterations in anatomy and ecology may only reflect prior biochemical changes.

Second Metamorphosis

The first requirement of a life cycle is that it be *circular*. Any organism that leaves its natal environment to explore, or grow up in, another must return at maturity to reproduce its kind. The spawning environment is fixed, whatever excursions animals may make as adults, and it is a truism that all animals must return to their natal environment to spawn.

For this reason, any animal that undergoes profound changes preparatory to migrating from its natal environment is likely to undergo a second series of changes in the reverse direction before

returning. Every metamorphosis invites a second metamorphosis.

Let us begin with the common spotted newt mentioned above. This animal begins its life as an olive-green, gilled larva, living wholly in the water. After several months it metamorphoses to a lung-breathing, land-dwelling eft. The color changes to a brilliant orange-red, the skin becomes rough and dry, the lateral-line organs recede (21). The newt now lives 2 to 3 years wholly on land, growing meanwhile almost to full size. Then it undergoes a second metamorphosis: the color returns approximately to that of the larva, and the newt regains the wet, shiny, mucus-covered skin, the keeled tail, the functional lateral-line organs, though not, of course, gills. In this mature state it reenters the water to spawn and live out the remainder of its life.

I have already said that the mature animal possesses porphyropsin, like a fresh-water fish. These animals, however, had already undergone the second metamorphosis. Red efts on examination were found to possess mixtures of rhodopsin and porphyropsin, predominantly rhodopsin (Fig. 11). The second metamorphosis in this species is accompanied therefore by the biochemical metamorphosis of its visual system from a predominantly land type to that characteristic of fresh-water types (8, p. 337).

This, in turn, brings us back to the sea lamprey. This animal has a life cycle

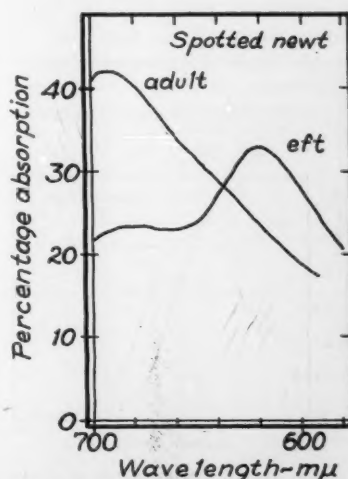


Fig. 11. Second metamorphosis of visual systems in the New England spotted newt, *Diemictylus viridescens*. Retinas of the land-living red eft contain a preponderance of vitamin A₁, with a minor admixture of A₂; retinas of water-phase, sexually mature adults contain vitamin A₂ predominantly or exclusively. [See Wald (8)]

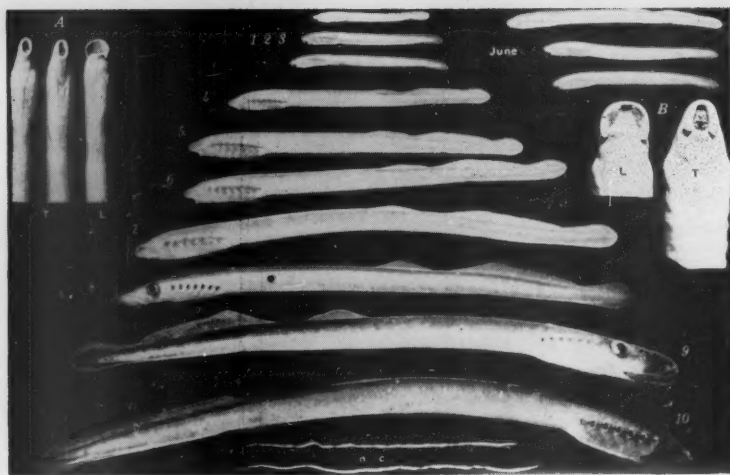


Fig. 12. Development of the sea lamprey, *Petromyzon marinus*. This animal begins its life in streams as a blind larva, buried in mud or sand (stages 1 to 7). Then it undergoes a first metamorphosis while still in this position (stages 8 to 10), preparatory to migrating downstream. Several years later it undergoes a second metamorphosis, to the sexually mature adult, and migrates upstream again to spawn and die. (A, B) Transformation of the mouth at first metamorphosis from the larval, hooded form (L) to the contracted circular form (T). (n c) Notochords of decayed adults found in streams after spawning. [From Gage (22)]

much like that of a salmon (Fig. 12). After passing 4 to 5 years as a blind ammocoete larva, living buried in the sand or mud of its natal stream, it undergoes, while still in that position, a profound metamorphosis, preparatory to migrating downstream to the ocean or a lake for its growth phase. This lasts $1\frac{1}{2}$ to $3\frac{1}{2}$ years. Then the sea lamprey undergoes a second metamorphosis, to the sexually mature adult. The sexes differentiate visibly for the first time: the gonads mature, secondary sex characteristics appear, the males develop a rope-like ridge along the back, and either sex

may assume golden mating tints. Then these animals migrate upstream to spawn (22).

Some years ago I found that the sea lamprey, taken on its spawning migration, has almost exclusively vitamin A_2 in its retina, and I concluded from this that it probably possesses porphyropsin (23). Since lampreys are members of the ancient class Agnatha, which includes the most primitive living vertebrates, I took this observation to support the view that porphyropsin is the ancestral type of visual pigment in vertebrates.

Recently, however, Crescitelli (24) reported that he had extracted rhodopsin from the retinas of this species and pointed out that this goes better with the opposed view, that rhodopsin is the primitive vertebrate pigment.

The specimens of sea lamprey examined by Crescitelli had just metamorphosed from the larval condition and had begun to migrate downstream, whereas the ones I had examined were at the other end of their life cycle, migrating upstream to spawn. On obtaining downstream migrants like Crescitelli's, I confirmed his observations exactly (Fig. 13). The retinas of such animals contain vitamin A and rhodopsin alone. The upstream migrants, however, possess vitamin A_2 and porphyropsin virtually alone (25). We find therefore in this most primitive group of vertebrates another biochemical example of second meta-

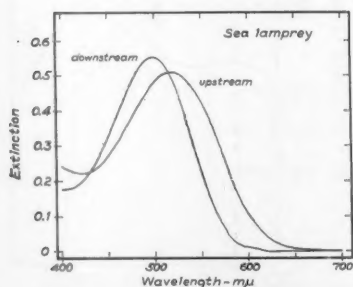


Fig. 13. Second metamorphosis of visual systems in the sea lamprey, *Petromyzon marinus*. The downstream migrants, having recently undergone the first metamorphosis from the larval stage, possess rhodopsin. The sexually mature adults, migrating upstream from the sea to spawn, have porphyropsin alone. [From Wald (25)]

morphosis, like that previously observed in the newt.

Such second metamorphoses expose fundamental characteristics of the metamorphic process:

1) Both the first and second metamorphoses anticipate changes in environment. Ordinarily they occur in the old environment and are completed there. They are preparations for the new environment, not responses to it.

2) Just as the first metamorphosis prepares the animal to leave its natal environment, so the second metamorphosis prepares it to return, completing the life cycle. It is of the essence of a second metamorphosis to reverse in part the changes which accompanied the first metamorphosis. The two metamorphoses tend to be opposed in direction, anatomically and biochemically.

3) Just as the changes in the first metamorphosis tend to have the character of recapitulations—that is, to coincide somewhat with the animal's evolutionary history—so the changes which occur in a second metamorphosis are likely to be antirecapitulatory, to reverse in direction the sequence of changes that accompanied the animal's evolution.

The last consideration involves a potential source of confusion. As I have already said, a life cycle is circular. If one section of it runs parallel with the course of evolution, another section is likely to run counter to that course. Just as every metamorphosis invites a second metamorphosis, so every associated recapitulation invites a subsequent antirecapitulation. This is only proper, provided it occurs at the point in the animal's history when it is being prepared for the return to the natal environment.

Deep-Sea Fishes; Eels

Heretofore I have discussed only changes in the visual pigments that involved their prosthetic groups. I should like now to discuss another type of change, involving the other component of a visual pigment, the protein opsin.

A short time ago Denton and Warren (26) reported that the visual pigments of deep-sea fishes, instead of having absorption maxima (λ_{max}) near 500 mμ, as do the rhodopsins of surface forms, have λ_{max} near 480 mμ. In consequence, they are orange in color rather than red, and Denton and Warren proposed that they be called chrysopsins, or visual gold. For reasons which appear below, I prefer to call them deep-sea rhodopsins.

This observation has since been confirmed by Munz (27) and by Wald, Brown, and Brown (28). It makes good ecological sense; for the surface light that penetrates most deeply into clear sea water is blue, and made up of wavelengths near 480 m μ , and the rhodopsins of deep-sea fishes are more effective through having their maximal absorption in this region of the spectrum (26).

As might be expected, the transition from surface to deep-sea rhodopsin is not sudden. A preliminary exploration shows that the absorption spectra of the rhodopsins shift more or less systematically with depth from the surface to about 200 fathoms (Fig. 14). We find that throughout such a series the prosthetic group—the retinene—remains the same. It is the opsin which alters (28). We have here a relationship comparable with that familiar in the hemoglobins, all of which possess the same heme joined with a variety of globins, different in every species.

Disregarding the relatively few rhodopsins and porphyropsins which lie in exceptional positions, one sees, therefore, a major transition (from λ_{\max} 480 to λ_{\max} 500 m μ) in the rhodopsins of marine fishes, correlated with depth, and depending on a systematic change of opsins; this connects with a further major transition from rhodopsin to porphyropsin (from λ_{\max} 500 to λ_{\max} 522 m μ) correlated with the transfer to fresh water, and depending on the change of chromophore from retinene₁ to retinene₂.

With this we can return to the "fresh-water" eel (*Anguilla*). Carlisle and Denton (29) have recently confirmed our observation that this animal, when taken in fresh water, ordinarily possesses the mixture of rhodopsin and porphyropsin described earlier; but they find that toward the beginning of its spawning migration it goes over to deep-sea rhodopsin (Fig. 15). Whereas the absorption peak of its usual mixture of visual pigments, when the eel is in fresh water, lies at about 505 m μ , that of the animal about to migrate lies close to 485 m μ . Indeed, the rhodopsin of such a "fresh-water" eel preparatory to migration is virtually identical in spectrum with that of the permanently deep-sea conger eel (30).

This is another instance of a second metamorphosis (Fig. 16). The eel, having been spawned in the depths of the Sargasso Sea, journeys as a larva (leptocephalus) to the shores of America or Europe (31). There it metamorphoses to the adult form and usually, though

probably not always, migrates into fresh water for its growth phase. Eventually it metamorphoses again: its color changes, the eyes approximately double in diameter, the digestive system deteriorates. As though getting ready for its return to the Sargasso Sea, it changes also to deep-sea rhodopsin.

My co-workers, Paul and Patricia

Brown, have recently examined such animals at the Stazione Zoologica in Naples (5). The European eel about to migrate seaward seems first to lose its retinal vitamin A₂ and retinene₂ and then to begin to combine vitamin A₁ and retinene, with a new, deep-sea opsin. The animal has already progressed far with this, as with the anatomical changes of

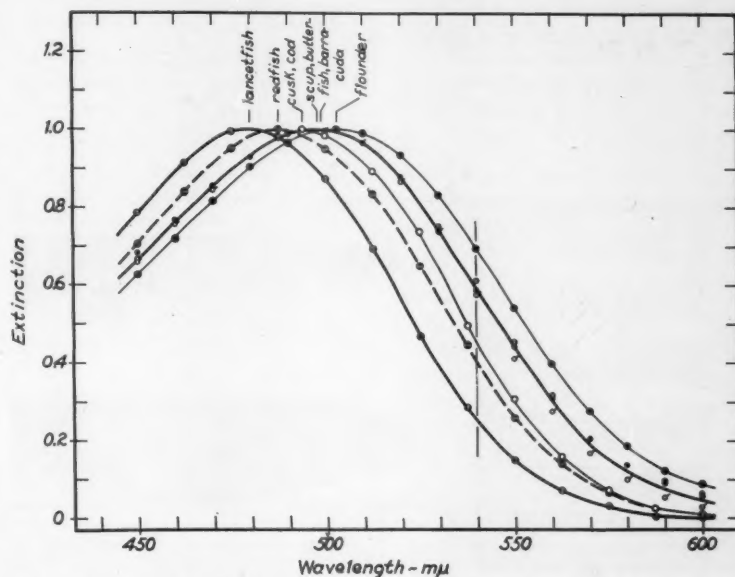


Fig. 14. The rhodopsins of fishes taken at various depths in the sea. That of the lancet fish, found ordinarily below 200 fathoms, has λ_{\max} about 480 m μ ; those of surface forms (scup, butterfish, barracuda, flounder) have λ_{\max} 498 to 503 m μ . The cusk and cod (from summer depths of 40 to 50 fathoms) have λ_{\max} 494 to 496 m μ , and the redfish (from a depth of about 100 fathoms) has λ_{\max} 488 m μ . [From Wald, Brown, and Brown (28)]

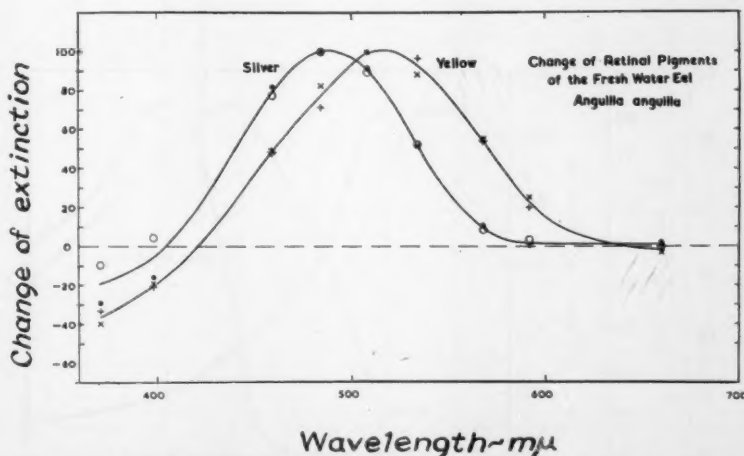


Fig. 15. Second metamorphosis of visual pigments in the European "fresh-water" eel. The yellow eel, prior to second metamorphosis, has a mixture of rhodopsin and porphyropsin (net λ_{\max} 500 to 505 m μ) corresponding to the mixture of vitamins A shown in Fig. 4. The sexually mature silver eel, about to begin its spawning migration to the Sargasso Sea, has changed over to deep-sea rhodopsin (λ_{\max} about 487 m μ) [Carlisle and Denton (29, 38)].

the second metamorphosis, while still in fresh water.

Such observations can tell us something concerning the larval condition. To my knowledge, no one has yet examined the visual pigment of the leptocephalus larva, but the foregoing discussion suggests strongly that the pigment is deep-sea rhodopsin. Similarly, though no one seems as yet to have examined the retinal pigment of the larval New England newt, our observation that the adult at maturity metamorphoses to porphyropsin implies that this is also the larval pigment. Again, since the blind ammocoete larva of the sea lamprey metamorphoses to an eyed adult possessing rhodopsin, this is the first visual pigment to appear in this

species. Yet the fact that in the second metamorphosis the pigment changes to porphyropsin implies that the latter represents the true, albeit missing, larval type. That is, since the second metamorphosis involves some measure of return to the larval condition, it can tell us something of the larval state, even of larval properties which have been lost in the course of evolution.

Land Vertebrates

Land vertebrates still pursue their embryogeny in water, but they have brought the water ashore. In a sense they are erstwhile amphibia which have carried wa-

ter ashore in which their embryos go through the larval stages and first metamorphosis. They have developed two special devices for this: the boxed-in or cleidoic egg, and viviparity. Amphibia still experiment with both. Certain of them—for example, the American red-backed, slimy, and worm salamanders—lay eggs on land within which the larvae complete their entire development. Others—such as the European black salamander, *Salamandra atra*—retain the eggs in the body until the young are fully formed. The European spotted salamander, *S. maculosa*, ordinarily lays its eggs in streams, but if it cannot reach water, permits them to develop internally.

One might hope, therefore, to find residues of metamorphosis in the embryogeny of land vertebrates, and in this one is not disappointed. Anatomical residues abound; they were the original source of the idea of recapitulation and were principally responsible for its early overexuberance. The embryo of a land vertebrate undergoes an anatomical metamorphosis approaching that of an amphibian. Unlike a larval amphibian, it never has functional gills; but, for a time, it does of course have gill slits, as well as other evidences of earlier aquatic life.

One finds biochemical metamorphosis also in the embryos of land vertebrates, and it includes some of the same changes with which metamorphosis in amphibia has already made us familiar.

So, for example, Joseph Needham (32) has shown that the chick embryo developing in the egg displays a changing pattern of nitrogen excretion (Fig. 17). It begins by excreting about 90 percent of its nitrogen as ammonia, like a fish; then changes to excreting up to 90 percent as urea, like most adult amphibia; and in the last stages of incubation excretes about 90 percent as uric acid, as do adult birds.

In general, vertebrates hold the osmotic pressures of their body fluids within narrow limits. In the various groups of vertebrates the blood osmotic pressure takes characteristic values, correlated to a degree with the ecology, and perhaps also with the phylogeny (see 8, p. 337). Thus, the freezing-point depression ($\Delta F.P.$) of the plasma in fresh-water fishes and amphibia lies at 0.45° to 0.55°C , whereas adult birds and mammals exhibit values of 0.55° to 0.65°C . Recent measurements in the developing chick (33) show that the fluids of the early embryo have freezing-point depressions at about 0.47°C (Fig. 18). The fluid osmotic pressure rises throughout development, with a final spurt at hatch-

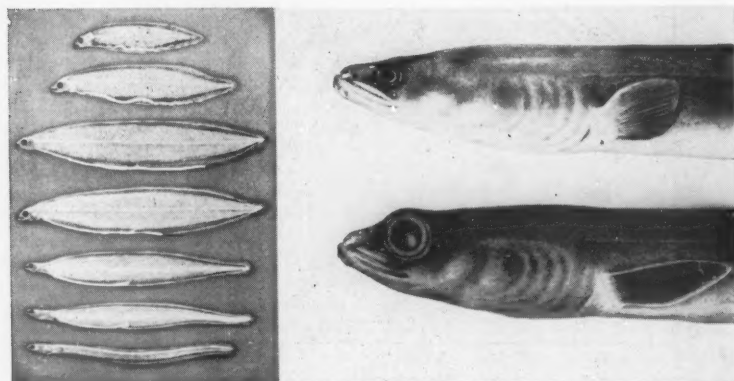


Fig. 16. Development of the American eel, *Anguilla rostrata*. (Left, top to bottom) Three larvae, or leptocephali, of various sizes; then three larvae undergoing the first metamorphosis; and the metamorphosed "glass eel." The uppermost three pictures are enlarged 2.7 times relative to the others. (Right) The second metamorphosis: (top) American eel in the "green" stage; (bottom) a European eel in the "silver" stage, ready for its spawning migration. Note particularly in the latter the approximate doubling in diameter of the eye. This large-eyed stage has not yet been observed in the American species. [From Vladyskov (37)]

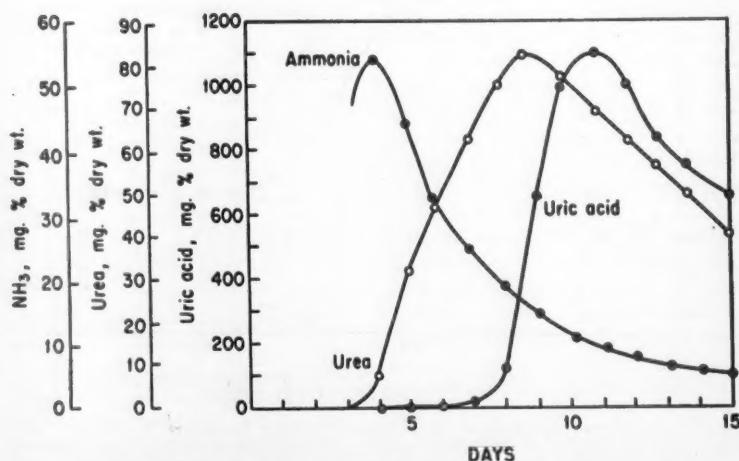


Fig. 17. Biochemical metamorphosis of nitrogen excretion in the developing chick. During incubation in the egg, the chick embryo successively excretes about 90 percent of its nitrogen as ammonia, then as urea, and finally as uric acid. [After Needham (32)]

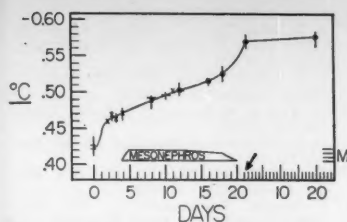


Fig. 18. Biochemical metamorphosis of fluid osmotic pressure in the developing chick. (Ordinates) Freezing-point depression, a measure of osmotic pressure; (abscissae) days of incubation, to hatching on the 21st day (arrow), and days thereafter; (—) unincubated egg white, (x) sub-germinal fluids, (—) amniotic fluids, (o) bloods. The embryo begins with osmotic pressures characteristic of fresh-water fishes and amphibia and ends with the much higher osmotic pressure characteristic of mature birds and mammals. The duration of functional activity of the mesonephros (M) is also indicated. [From Howard (33)]

ing that brings it to the adult value (Δ F.P. = 0.58°C). That is, the embryo begins with a fluid osmotic pressure characteristic of fresh-water fishes and amphibia and ends with that characteristic of mature birds (34).

Again, Hall (35) has shown that during the embryonic development of the chick its hemoglobin changes radically, continuously losing affinity for oxygen, so that in an adult chicken more than twice the oxygen pressure is needed for half-saturation than is needed in a ten-day-old chick (Fig. 19). These changes persist for some time after hatching. They are similar in direction to the change in hemoglobin that accompanies metamorphosis in the bullfrog.

Comparable changes in hemoglobin accompany the embryonic development of all mammals so far examined. It is now well recognized that in mammals generally, man included, fetal hemoglobin is a different species of molecule from maternal or adult hemoglobin (see 36) (Fig. 20). Always—with the possible exception of man—the change in oxygen affinity is in the same direction, a loss of affinity as development progresses. The fetal and adult hemoglobins of mammals differ also in many other ways: in electrophoretic mobility, sedimentation rate, resistance to alkali, immunological specificity, solubility, crystal shape, and amino acid composition (see 8, references). All these changes involve the

globin moiety of hemoglobin; the heme is the same always.

The phenomenon of metamorphosis, biochemical as well as anatomical, extends therefore beyond the amphibia and fishes to include the land vertebrates, both egg-laying and placental.

Do land vertebrates exhibit also vestiges of a second metamorphosis? I suppose that puberty is so to be regarded. To be sure, this does not prepare a land vertebrate to migrate, for the natal environment is now segregated, and puberty prepares the animal only to mate. Here only one representative cell—the spermatozoon—completes the return to the natal environment; and this, of course, undergoes a profound metamorphosis before being launched upon a migration as formidable, relative to its size, as that of any salmon.

Conclusion

Metamorphosis is a basic and general phenomenon, common to the whole vertebrate stock. It includes anatomical, physiological, and—perhaps prior to these—biochemical components, all de-

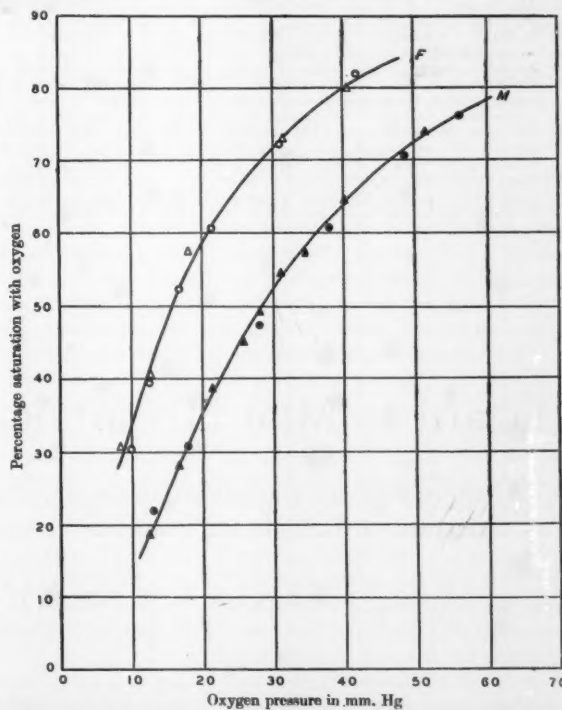
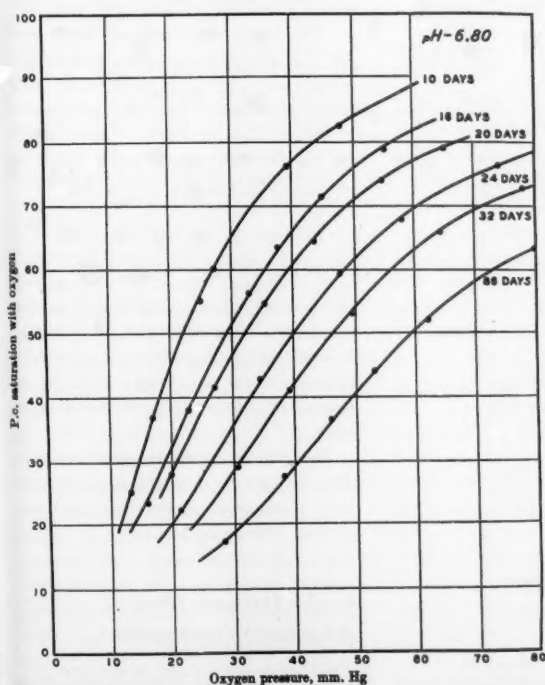


Fig. 19 (left). Biochemical metamorphosis of hemoglobin during development of the chick. Measurements on dilute solutions of hemoglobin buffered at pH 6.80 and equilibrated with oxygen at 37°C . The affinity for oxygen decreases regularly from the tenth day of incubation, and this change continues for some time after hatching. [From Hall (35)]. Fig. 20 (right). Biochemical metamorphosis of hemoglobin in a placental mammal. Oxygen equilibrium curves of hemoglobin from a goat fetus (F) and from the mother (M). The fetal hemoglobin has almost twice as high an affinity for oxygen as the maternal, measured in solution at 37°C and pH 6.8. Both hemoglobins were obtained at 15 to 18 weeks' gestation. [From Hall (36)]

signed to prepare the animal to leave its natal environment. Necessarily, in order to reproduce, the animal must eventually return, so completing its life cycle; and its return may be prepared for by a second metamorphosis, in some aspects the reverse of the first.

Our history as vertebrates is not dust to dust but water to water. From this point of view Nicodemus' great question can be given a broad and positive biological answer. Every animal can and must return to the "womb"—not, indeed, to be born again, but to bear the next generation. For a catadromous fish, the "womb" is the sea; for anadromous fishes and amphibia, a pond or stream; for land vertebrates, a uterus or egg. The question raises additional problems only for man, and then only when the sense of return is toward the womb of the mother rather than that of the mate.

References and Notes

1. The investigations from the Harvard laboratory reported in this article were supported in part by the Rockefeller Foundation and The Office of Naval Research. This article is based on a lecture given 16 April 1958 at the annual dinner of the American Society for Pharmacology and Experimental Therapeutics.
2. G. Wald, *Am. J. Ophthalmol.* 40, 18 (1955); —, in *Enzymes: Units of Biological Structure and Function*, O. H. Gaebler, Ed. (Academic Press, New York, 1956), p. 355; R. A. Morton and G. A. J. Pitt, *Fortschr. Chem. org. Naturstoffe* 14, 244 (1957).
3. G. Wald, *J. Gen. Physiol.* 22, 391 (1938–39).
4. —, *ibid.* 22, 775 (1938–39).
5. Recent experiments in our laboratory and at the Stazione Zoologica in Naples by P. K. Brown and P. S. Brown have shown that there is considerable variation in the proportions of vitamins A₁ and A₂ in the retinas of individual immature eels, of both the American and European species, these proportions varying between 65:35 and 25:75, with a mean value of approximate equality. The visual pigments, rhodopsin and porphyropsin, are present in approximately the same molar ratios; but since rhodopsin possesses a higher specific extinction than porphyropsin (about 4:3), extinctionwise rhodopsin tends to predominate.
6. G. Wald, *J. Gen. Physiol.* 25, 235 (1941–42).
7. The "ultimately" here conceals a thorny problem. Fish evolution has probably involved numerous interchanges between fresh-water and marine existence, and many present-day fresh-water bony fishes may have had marine forms in their ancestry. In that case one should have to assume that the complex of genetic changes that has brought stocks into fresh water has regularly carried with it the property of using vitamin A₂ and porphyropsin in vision. I cannot suggest a mechanism for this association; the association itself is a fact to which as yet no exceptions are known.
8. G. Wald, "Biochemical evolution," in *Modern Trends in Physiology and Biochemistry*, E. S. G. Barron, Ed. (Academic Press, New York, 1952).
9. —, *Harvey Lectures Ser.* 41, 117 (1945–46).
10. F. H. Wilt has recently confirmed these observations and has found that if metamorphosis is induced prematurely with thyroxine, the visual system also changes prematurely [cited in "Annual Report, Director, Department of Embryology," *Carnegie Inst. Wash. Year Book* 56, 299 (1956–57); also personal communication].
11. F. H. McCutcheon, *J. Cellular Comp. Physiol.* 8, 63 (1936).
12. A. F. Riggs, *J. Gen. Physiol.* 35, 23 (1951–52).
13. C. Manwell [*Science* 126, 1175 (1957)] has reported finding differences in the alkaline denaturation of hemoglobin in the postlarval and adult California sculpin (*Scorpaenichthys marmoratus*), a marine teleost. He states also that preliminary experiments on a live-bearing surf perch (*Embiotoca lateralis*) reveal a fetal form of hemoglobin by alkaline denaturation.
14. E. Frieden, A. E. Herner, L. Fish, E. J. C. Lewis, *Science* 126, 559 (1957).
15. A. F. Munro, *Biochem. J.* 33, 1957 (1939).
16. —, *ibid.* 54, 29 (1953).
17. G. Wald and D. W. Allen, *J. Gen. Physiol.* 40, 593 (1956–57).
18. H. J. A. Dartnall, *J. Physiol.* 125, 25 (1954); G. Wald, *Nature* 175, 390 (1955).
19. E. E. Underhay and E. Baldwin, *Biochem. J.* 61, 544 (1955).
20. M. M. Cragg, Ph.D. thesis, University of London (1953), cited in E. E. Underhay and E. Baldwin, *Biochem. J.* 61, 544 (1955).
21. A. B. Dawson, *J. Exptl. Zool.* 74, 221 (1936).
22. S. H. Gage, "The lampreys of New York State," in "Biological Survey of the Oswego River System," *N.Y. State Conserv. Dept. Biol. Survey Suppl. Ann. Rept.* (1927), p. 158.
23. G. Wald, *J. Gen. Physiol.* 25, 331 (1941–42).
24. F. Crescitelli, *ibid.* 39, 423 (1955–56).
25. G. Wald, *ibid.* 40, 901 (1956–57).
26. E. J. Denton and F. J. Warren, *Nature* 178, 1059 (1956); *J. Marine Biol. Assoc. United Kingdom* 36, 651 (1957).
27. F. W. Munz, *Science* 125, 1142 (1957); *J. Physiol. London* 140, 220 (1958).
28. G. Wald, P. K. Brown, P. S. Brown, *Nature* 180, 969 (1957).
29. D. Carlisle and E. J. Denton, *J. Physiol. London* 139, 8P (1957).
30. E. J. Denton and M. A. Walker, *Proc. Roy. Soc. London* 148B, 257 (1958).
31. J. Schmidt, *Smithsonian Inst. Ann. Rept.* (1924), p. 279; *Phil. Trans. Roy. Soc. London*, 211B, 179 (1922).
32. J. Needham, *Biol. Revs. Biol. Proc. Cambridge Phil. Soc.* 5, 142 (1930). See, however, the later experiments of J. Needham, J. Brachet, and R. K. Brown [*J. Exptl. Biol.* 12, 321 (1935)], and particularly those of J. R. Fisher and R. E. Eakin [*J. Embryol. and Exptl. Morphol.* 5, 215 (1957)], according to which the ammonia content of the whole egg may stay relatively constant from days 0 to 13 of incubation—that is, ammonia is neither formed nor "excreted" during this period; and urea is formed in the developing chick, not from ammonia by an ornithine cycle, but from pre-existing arginine through hydrolysis by arginase.
33. E. Howard, *J. Cellular Comp. Physiol.* 50, 451 (1957).
34. This may be an example of a more general phenomenon. In the frog *Rana temporaria*, the ovarian eggs have an osmotic pressure like that of adult blood (Δ F.P., 0.41°C). Within a few hours after fertilization this has fallen to about 0.33°C and in the gastrula stage reaches the extraordinarily low minimum of 0.275°C. Then it rises again, so that toward the end of the first week of development it again approaches the adult level [A. Krogh, K. Schmidt-Nielsen, E. Zeuthen, *Z. vergleich. Physiol.* 26, 230 (1938–39); see also [E. L. Backman and J. Runnström, *Biochem. Z.* 22, 290 (1909), and K. Bialasiewicz, *Arch. Entwicklungsmech.* 34, 489 (1912)]. I hardly know whether these changes in frogs and chicks are properly to be described as "metamorphoses." They may come too early in development and may be too continuous for that. I include them tentatively in this discussion in the hope that further examination will clarify their status.
35. F. G. Hall, *J. Physiol. London* 83, 222 (1934–35).
36. —, *ibid.* 82, 33 (1934).
37. V. D. Vladyskov, "The eel," in "Fishes of Quebec," *Publ. Quebec Dept. Fisheries* (1955).
38. For this figure, showing as yet unpublished measurements of Carlisle and Denton (29), I am very grateful to Dr. E. J. Denton.

Hazard to Man of Carbon-14

What problems are encountered in the quantitative estimation of the biological hazards of carbon-14?

John R. Totter, M. R. Zelle, H. Hollister

Carbon-14 is an isotope of the chemical element carbon. As such, it forms the same chemical compounds and, as part of the organic molecules built around the carbon atom, becomes part of living tissue. Carbon-14, though vir-

tually indistinguishable chemically from the other isotopes of carbon, is radioactive, emitting low-energy beta particles (0.05 Mev average) and having a half-life of about 5600 years. Therefore, carbon-14 is a potential hazard to man, for

in his body it is emitting radiation that can affect living cells and, additionally, is itself undergoing change—transmutation—by decay to another element, nitrogen, of different chemical characteristics.

This article considers briefly some of the problems encountered in the quantitative estimation of the biological hazards to man of carbon-14.

Possible Mutagenic Effect of Carbon-14 Transmutation

Most discussions of the genetic effects of radioactive isotopes present in the body have considered only the effects of the radiation emitted during radioactive decay. However, the transmutation of radioactive atoms which have been

incorporated into the genetic material, deoxyribonucleic acid (DNA), may also result in mutations. Radioactive isotopes of carbon, phosphorus, and hydrogen must all be considered, but, since nuclear detonations may produce appreciable amounts of carbon-14, this long-lived isotope is of particular concern. On the molecular scale, mutations are believed to be changes in the chemical structure of DNA.

When a carbon-14 atom contained in DNA decays to nitrogen-14 by the emission of a beta particle, a mutation could result in two ways: (i) by a radiochemical change in DNA caused by either the beta particle emitted or by recoil of the nucleus and (ii) as a result of the carbon-14 to nitrogen-14 transmutation itself, which almost certainly would cause a chemical change in the DNA molecule in which it occurred. Since all DNA is contained in the chromosomes and is genetically active, it is possible that almost all such transmutations occurring in DNA would cause mutations. On the other hand, it is conceivable that the chemical changes caused by transmutation of carbon-14 in DNA would prevent the successful duplication of the DNA and hence would be lethal to the cell in which the transmutation occurred, with the result that no detectable mutations would be produced.

There are almost no data as yet on which to base an estimate of the magnitude of the transmutation effect. Experiments made to obtain such data must be carefully planned to differentiate between mutations produced by the two processes and are complicated further by the long half-life and low specific activity of the available carbon-14 isotope preparations. Certain microorganisms appear to offer the most promising experimental approach.

The natural carbon-14 content of the biosphere is given by Anderson (1) as 1.46×10^{-12} times the total carbon content. The three isotopes of carbon are uniformly distributed in the atmosphere and in living organisms, so one can estimate the contribution which the disintegration of carbon-14 makes to the total radiation dose. Since the transmutation of an element such as carbon or phosphorus in the chain of DNA is probably much more effective in producing bio-

logical damage, the carbon-14 content of DNA is of interest.

Mammalian diploid cells contain 6 to 7×10^{-12} gram of DNA per cell (2), and DNA is approximately 37 percent carbon. Therefore each diploid cell contains about 2.4×10^{-12} gram of DNA carbon. A carbon atom weighs $12/(6 \times 10^{23}) = 2 \times 10^{-23}$ gram, and each diploid cell's DNA should contain $(2.4 \times 10^{-12})/(2 \times 10^{-23}) = 1.2 \times 10^{11}$ atoms. The carbon-14 content is $1.2 \times 10^{11} \times 1.28 \times 10^{-12} = 1.54 \times 10^{-1}$ atom per cell in DNA. That is, on the average, about one in six cells should contain a carbon-14 atom in the DNA.

The probability that each cell would suffer a carbon-14 transmutation is given by dividing the average life of carbon-14 (about 8000 years) into 1.54×10^{-1} :

$$\frac{1.54 \times 10^{-1}}{8.0 \times 10^3 \text{ yr}} = 1.9 \times 10^{-5}$$

per year. The generative cells may be assumed, on the average, to have accumulated 30 years of this kind of damage at conception time. That is, the probability that any given generative cell has had a carbon-14 transmutation in its genetic material is 6×10^{-4} .

With a birth rate of 30 per 1000 and 2.5×10^9 as the world population, the maximum genetic damage from carbon-14 transmutations in genetic material could result in the birth, each year, of $2.5 \times 10^9 \times 3 \times 10^{-2} \times 6 \times 10^{-4} = 4.5 \times 10^4$ persons with mutated genes. This assumes a ratio of 1 for the fraction mutations/transmutations (M/T).

In his estimates of fission-product and carbon-14 hazards, Leipunsky (3) assumed an increment of carbon-14 due to 10 megatons of fusion equal to 4.1×10^{-8} times the present carbon-14 equilibrium value. Such a value would yield $4.1 \times 10^{-8} \times 4.5 \times 10^4 \times 8100 = 1,400,000$ persons with defective genes due to the carbon-14 increment. One-half of these defects would occur in the 5600 years following the addition of the carbon-14 increment. It is possible that the value of 4.1×10^{-8} may be too large by a factor as great as 10. As was indicated by Libby (4), one-fourth of this value, or 10^{-8} , would be more correct. If we were to assume a reduction by a factor of 10, the figures would reduce to a total of 144,000.

The fractional increase per year cannot be given because of the exponential decrease in carbon-14, but the maximum fractional increase due to fusion-produced carbon-14, assuming immediate complete mixing, would be 184/45,000 in one case and 18/45,000 in the other.

This ratio, of course, is valid no matter what the value of M/T .

Some limits on the possible values of M/T may be set. Although it is conceivable that more than one mutant gene might result from one transmutation, this is not likely to be a frequent occurrence. Only about one-half of the carbon atoms of DNA are in the chain, and a fraction of the remaining half may be less likely to cause mutations when decay takes place. More important, the decays may be so effective as to totally inactivate the cell, in which case no mutation will result. Therefore, the upper limit would appear to be set safely at less than 1.

There appears to be no logical or experimental basis on which to base an estimate of the lower limit of the fraction M/T . When inactivation of *Neurospora* and bacterial viruses was measured (see 5), experimental values for phosphorus-32 decay were between 10 and 1000 times greater than values for the probability of inactivation by comparable amounts of ionization. There appear to be no data for production of mutations by transmutation of carbon-14 or phosphorus-32 in DNA. McQuade, Friedkin, and Atchison (6) have provided data on chromosome aberrations due to thymidine-2-carbon-14 incorporation in which the carbon-14 decay in DNA appears to be at least 9 or 10 times as effective as decay in cytoplasm. However, the data are inconclusive, as was pointed out by the authors themselves.

It is of interest to calculate the value of M/T which would result in a mutation frequency due to carbon-14 transmutation in DNA which is equal to the mutation frequency from the ionization produced by carbon-14 decay outside the DNA. This value is equal to the ratio of beta radiation mutations to the mutations resulting from carbon-14 transmutations in DNA on the hypothesis that $M/T=1$. Leipunsky (3) estimated 49,000 mutations from beta radiation where our corresponding carbon-14 transmutation estimate is 1.44×10^6 . This leads to $M/T = 0.034$ for the value for equal numbers of mutations for the two processes. If one uses more refined estimates of the carbon-14 beta radiation dose, this value would not be changed, since estimates of both the beta dose and the number of carbon-14 transmutations depend on the bomb-produced increment to the natural carbon-14 pool.

This ratio, 0.034, depends on beta-induced mutations of only one class, serious physical or mental defect, with an estimated normal frequency of 2 percent.

Dr. Zelle and Mr. Hollister are on the staff of the Division of Biology and Medicine, U.S. Atomic Energy Commission, Washington, D.C. Dr. Totter, a former member of the same staff, is presently at the University of Montevideo, Montevideo, Uruguay. This article is a reprint, with minor editorial alterations, of "The biological hazard to man from carbon-14 from nuclear weapons," U.S. Atomic Energy Commission USAEC WASH-1008 (Sept. 1958).

If one includes all three classes of genetic damage considered by Crow (7), two of which are partially overlapping, the value of M/T necessary for equal transmutation and beta-induced mutation frequencies is 0.66.

It is therefore concluded that, on the basis of limited experience in other organisms and with other isotopes, it is not unreasonable to assume that the number of mutations due to carbon-14 disintegration in DNA could be at least equal to, and could probably exceed, the number caused by the carbon-14 beta radiation.

There is some evidence that genes in different species differ in size and complexity. For example, Carter (8) estimates that each gene in the mouse is 19 times as large as a *Drosophila* gene. This estimate is based on comparative mutation rates and the 29-fold greater DNA content per diploid cell in mice. If this conclusion is correct, the value M/T for any species can be accurately determined only by experiment on that species, and the effects in mice and other mammals may be very much more serious than those in microorganisms, for example. However, the greater DNA content could conceivably consist largely of "nongenic" DNA, in which carbon-14 decay would be less apt to cause mutation. Thus, it is possible to do no more now than guess at the broad limits of the ratio M/T .

Numerical Estimation of Genetic Damage to Human Populations

With the advent of atomic and nuclear energy, the question of genetic hazards has become a matter of great importance, of almost universal interest, and of no little controversy. In the past 2 years there have been three comprehensive statements of the present status of knowledge concerning the problem (9-11), and there will soon be a fourth (12). All of these statements agree about the seriousness of the problem, about the lack of sufficient knowledge of human spontaneous and radiation-induced mutation rates to provide accurate numerical estimates of the hazards, and about the desirability of minimizing the exposure of human reproductive cells to radiation during the reproductive period. The reports are in agreement also on the conclusion that the linear mutation-dose relation observed in the range of 25 to several thousand roentgens in a number of species must be considered to extend through smaller doses to zero. In other words, it is concluded that there

Table 1. Estimates of damage from fallout calculated by J. F. Crow and presented at hearings of the Special Subcommittee on Radiation, U.S. Congress, in 1957 (7).

Kind of damage	No.	
	First generation	Total
A. Gross physical or mental defect	8,000	80,000
B. Stillbirths and childhood deaths	20,000	300,000
C. Embryonic and neonatal deaths	40,000	700,000

is no dose of radiation so small that it is not genetically harmful.

Since, therefore, the number of mutations induced is considered to be directly proportional to the radiation dose, it is possible to make crude numerical estimates of the hazards, provided information is available on the average dose to the gonads during the reproductive period. Many geneticists feel that it is unwise to make such calculations, since there is a very high degree of uncertainty in them and, consequently, the calculations may be quite misleading or may be misinterpreted. However, since such calculations have been and will be made frequently, it is important to recognize the assumptions on which they are based and the sources of uncertainty in the results.

The usual approach to the calculations involves use of the doubling dose, or that dose required to induce mutations at a rate equal to the spontaneous or natural rate. This dose is usually taken as 50 roentgens, although the National Academy of Sciences (9) and Medical Research Council (10) reports give only the range 30 to 80 roentgens. A draft of the more recent consideration by the United Nations Scientific Subcommittee (12) gives a range of 10 to 100 roentgens. This large factor of uncertainty must be constantly borne in mind when one is considering the results of such calculations.

The usual calculation is concerned only with rather gross, tangible genetic effects, as considered in the National Academy report (9), and ignores the completely recessive mutations or the probably much larger class of mutations with small effects which nevertheless are harmful. The estimates are therefore almost certainly underestimates of the total damage. It is also important to keep in mind the question of genetic equilibrium. With appropriate corrections for changes in population size, each unfavorable gene,

no matter how large or small in effect, induced in a population must be balanced in a subsequent generation by an elimination of a gene descended from that gene; otherwise, the frequency of that gene will increase cumulatively. Reduced effective fertility is the mechanism by which such eliminations occur. This can be thought of as a reduction in the chance that individuals, starting at the time of fertilization of the egg, will complete normal reproductive cycles. Thus, in a population in equilibrium, the total of reductions in fertility could be estimated to a first approximation if all unfavorable mutations—regardless of the magnitude of their unfavorable effect—could be individually detected and counted.

Perhaps the most useful calculations which have been made are those of Crow in the Fallout Hearings (7). His estimates are shown in Table 1. All of these estimates assume a 30-year dose to the gonads from fallout of 0.1 roentgen, as estimated in the National Academy report (9), a doubling dose of 50 roentgens, and a stable world population of 2×10^9 births per generation.

The gross physical or mental defect estimate ignored all completely recessive effects and assumed a normal incidence due to spontaneous mutation of 2 percent. This category roughly corresponds to the "tangible genetic defect" category of the National Academy report (9) and is perhaps the most useful kind of calculation for comparative purposes. The arithmetic is simple:

$$\left(\frac{0.1 \text{ r}}{50 \text{ r}}\right) (0.02) (2 \times 10^9) = 8 \times 10^4 \text{ (total)}$$

Stillbirths and childhood deaths were estimated from increased death rates in children of consanguineous marriages by Morton, Crow, and Muller (13), who give an estimate of 8 percent as the frequency at mutational equilibrium. As before, the total damage from 0.1 roentgen for a generation is obtained by

$$\left(\frac{0.1 \text{ r}}{50 \text{ r}}\right) (0.08) (2 \times 10^9) = 3.2 \times 10^5$$

This result was rounded to 3×10^5 .

The estimates of embryonic and neonatal deaths were based on Russell's (14) observation of a 3 percent reduction in litter size of mice at 3 weeks of age when the sires had been exposed to 300 roentgens. If both parents received 0.1 roentgen, the effect would be 0.2/300 as great. Hence, the estimated first-generation effect is

$$\left(\frac{0.2}{300}\right) (.03) (2 \times 10^9) = 4 \times 10^4$$

If it is assumed that 6 percent are expressed in the first generation, as estimated for stillbirths and childhood deaths, the total damage is approximately 6.7×10^8 , which rounds to 7×10^8 .

It is interesting to observe at this point that, although the numbers 80,000, 300,000, and 700,000 are large and obviously serious when it is remembered they assume an average gonadal dose of only 0.1 roentgen per generation, the estimated increase in the first generation in each case is only 10^{-4} of the normally occurring abnormalities. So small an increase would be impossible to detect experimentally. It is this apparent contradiction—large absolute numbers but small fractional increases—which leads to much of the controversy on this important question.

It is important to remember also that the second and third categories of damage are not mutually exclusive: stillbirths and infant deaths are included in both.

It is a simple matter to adjust Crow's figures for other doses or population sizes. This is illustrated in a later section, after a discussion of the gonadal exposures due to bomb-produced and natural carbon-14.

However, attention is again directed to the large uncertainty, perhaps as large as a factor of 10, in the doubling dose; this uncertainty, coupled with uncertainty in the spontaneous mutation rates, makes any conclusions that are drawn from such calculations correspondingly uncertain with respect to absolute magnitude. Even so, such calculations can be useful for comparative purposes, since these uncertainties affect each calculation equally and hence essentially cancel out. Therefore, the largest uncertainty in such comparisons derives from the calculations of the relative gonadal doses and, in the case of certain isotopes, our almost complete lack of information about the magnitude of the transmutation effect. It should also be borne in mind that estimates of "serious physical or mental defect," in Crow's terms (7), or of "tangible genetic defect," in the language of the National Academy report (9), do not measure the total genetic damage because certain categories of genetic damage are omitted from these calculations.

Biological Hazards

The natural occurrence of carbon-14. Carbon-14 is produced in nature in amounts estimated (9) to be from 7 to 10 kilograms per year by the absorption

of cosmic ray neutrons in the atmosphere. It exists in the atmosphere as radioactive carbon dioxide and as such takes part in the over-all carbon cycle of the earth, mixing with ocean water (existing there as a carbonate or bicarbonate) and with the biosphere (plants and animals) and entering man. Because carbon-14 appears to have existed naturally for millions of years or more, it now exists on earth in essentially a constant quantity (15): whatever is made each year only compensates, approximately, for what decays. Estimates of the amount of naturally existing carbon-14 in the total earth reservoir (ocean, biosphere, and atmosphere) range from about 56 to 81 metric tons by weight (3, 9, 15).

The approximate distribution of the 56 to 81 metric tons of natural carbon-14 in the earth's reservoir is shown in Table 2 (9). Because the distribution as well as the quantity of natural carbon-14 is important, Table 3, based on data presented by Arnold and Anderson (15), is presented to give an estimate of the distribution of all carbon in the earth's reservoir.

In all precise estimates of the natural background radiation dose to man, the contribution of natural carbon-14 is included, although its contributions to the estimated annual background dose of 100 to 150 milliroentgens (9, 16) is only about 1 percent (16).

Production of carbon-14 by nuclear weapon explosions. All nuclear weapons involve in their nuclear reactions the production of neutrons. Some of the neutrons are used in fission chain reactions resulting in the formation of radioactive fission products such as strontium-90, iodine-131, and cesium-137. The neutrons themselves would be of no concern, from the standpoint of hazards, were it not for the fact that some of them escape from the weapon to the outside environment. These neutrons of various energies are eventually captured; it is estimated that, for an air burst more than a few hundred meters above the ground, more than 95 percent of the neutrons eventually react with the nitrogen nuclei of the atmosphere and produce carbon-14. If the detonations are on the surface, then roughly one-half of the neutrons would not be absorbed in nitrogen atoms to make carbon-14 but, by the same token, would induce radioactivity of relatively short half-life in the soil.

For United States nuclear weapons of all types (17), roughly equal numbers of neutrons escape per unit of energy yield ("kiloton" or "megaton"). Therefore,

two nuclear weapons, regardless of type but of the same yield and detonated under the same conditions, will produce roughly equal amounts and types of neutron-induced radioactive materials, including carbon-14, if the burst is such that neutrons escape to the air.

In a recent speech, Libby (4) stated: "At a rate of 2.5 neutrons [escaping] per 200 Mev of energy release, one megaton would generate 3.2×10^{26} carbon-14 atoms. The best estimate, keeping in mind that a substantial amount [of the carbon-14 produced] falls back as calcium carbonate, would be that about 10^{28} carbon-14 atoms have been introduced into the atmosphere [from weapon testing to date], mostly into the stratosphere. The estimate of 2.5 neutrons per 200 Mev energy released is higher than an earlier estimate based on an assumed 15 percent escape efficiency [(17)], the later value being based on firmer information. It also attempts to weigh fusion and fission as they have actually occurred."

Leipunsky (3) has assumed for his fusion weapon one employing only deuterium-tritium fusion reactions and allowing all neutrons produced to escape to their environment. His estimate of the number of escaping neutrons per 200 Mev may be too high by a factor of 4 to 6 compared with like estimates for U.S. weapons.

The calcium carbonate represents an addition to the earth's carbon-14 reser-

Table 2. Approximate distribution of natural carbon-14 in the earth's reservoir.

Reservoir	Carbon-14	
	Metric tons	Percent
Atmospheric CO ₂	0.96	1.69
Terrestrial living matter plus humus	2.2	3.88
Ocean: total organic matter	3.8	6.7
Ocean: total inorganic matter	49.8	87.8
Total	56.8	100.07

Table 3. Estimated distribution of all carbon in the earth's reservoir.

Reservoir	Percent
Atmospheric CO ₂	1.47
Terrestrial living matter plus humus	2.83
Ocean: total organic matter	8.61
Ocean: total inorganic matter	87.2
Total	100.11

Table 4. Estimates of total genetic hazards of bomb-produced and natural carbon-14 and natural background radiation. (To estimate the hazard for the next 5000 years, divide these numbers by 2.) Categories B and C are partially overlapping.

Bomb C ¹⁴ to date (dose: 0.008 mr/yr)		Natural background radiation			
		Carbon-14 (dose: 1.5 mr/yr)		Total (dose: 150 mr/yr)	
Persons (No.)	Fraction of total population affected	Persons (No.)	Fraction of total population affected	Persons (No.)	Fraction of total population affected
1.0 × 10 ⁸	1/5,340,000	1.92 × 10 ⁷	1/27,800	9.6 × 10 ⁸	1/556
3.8 × 10 ⁸	1/1,400,000	7.2 × 10 ⁷	1/7,400	3.6 × 10 ⁹	1/148
9.0 × 10 ⁸	1/593,000	1.68 × 10 ⁸	1/1,785	8.4 × 10 ⁹	1/64

voir too, but in a chemical form such that the radiocarbon cannot exchange readily with the biosphere. One might note that 3.2×10^{26} carbon-14 atoms is about 7.4 kilograms and that 10^{28} carbon-14 atoms is about 230 kilograms. The addition of 230 kilograms (0.23 metric tons) of bomb-produced carbon-14 to date thus means an addition of 0.3 to 0.4 percent to the total carbon-14 reservoir.

However, this addition is not instantaneously uniform throughout the whole reservoir, for equilibrating time must be taken into account. All of the bomb-produced carbon-14, at the time it is produced, is in the atmosphere except for the direct fallback of calcium carbonate. The bomb-produced carbon-14 present in the atmosphere as carbon-14 dioxide can exchange with the biosphere and with the ocean. The higher the concentration of carbon-14 in the atmosphere, the higher will be the resulting concentration in plants after exchange. Eventually the exchange with the ocean will reduce the atmospheric level of bomb-produced carbon-14 concentration and so will reduce the opportunity for exchange with plants. Hence one is dealing with a transient, not an equilibrium, situation, and merely computing the fractional increase in the total carbon-14 reservoir caused by adding bomb-produced carbon-14 may not give a good measure of the impact of the bomb-produced carbon-14 on man but would tend to give too low an estimate. Libby states (18), "Bomb tests to date have produced enough carbon-14 so that when it has come to mixing equilibrium it will have increased the amount naturally present in all living matter by one-third of 1 percent"; and, "In the years before equilibrium with the deep ocean is

reached—about 500 years—the level will temporarily rest at about a 3 percent increase. . . . This is after the first period of perhaps ten or twenty years before dilution in the top layer of the ocean and with living and dead organic matter occurs, when the increase will be about 20 percent." Finally, he says, "Because the lifetime of radiocarbon is very long—8000 years on the average—the equilibrium situation is the more significant." For the carbon-14 already produced by bombs, the average dose increment over 8000 years is about 1.7 times the average dose increment calculated on the assumption of immediate equilibrium.

Carbon-14 dose to man. Libby (16) estimates the dose to man from naturally occurring carbon-14 as 1.5 milliroentgens per year. If no further bomb carbon-14 was produced, this dose rate might be as high as 1.8 milliroentgens per year during the next 20 years or so; after that time it would gradually drop off to a new equilibrium value of 1.505 milliroentgens per year. The average dose rate over 8000 years would be about 1.508 milliroentgens per year, yielding a total dose increment due to bomb-produced carbon-14 of 64 milliroentgens.

These dose estimates suggest that the present bomb-produced carbon-14 hazard to man is not only small but virtually undetectable: a 0.5 percent increase in a dose rate that itself is only 1 percent of the natural background radiation dose to man. Why, then, is bomb-produced carbon-14 possibly a concern? The answer is that genetic mutation rates, and possibly some somatic-effect incidence rates [for example, leukemia (19)], are considered to be linearly proportional to total dose. On this basis, therefore, any increase in the dose to man implies a corresponding increase in the burden of

mutations in the population, and possibly an increase in certain somatic effects such as leukemia.

Numerical estimation of the genetic effects of bomb-produced carbon-14. By means of the methods discussed earlier, it is easy to compare the estimated genetic effect of the carbon-14 produced by nuclear detonations to date with the estimated effects of the naturally occurring carbon-14 and the total natural background radiation (Table 4). The natural background radiation of 150 milliroentgens is essentially that estimated in the National Academy report (9). The natural and bomb-produced carbon-14 doses have been discussed above. An average life of carbon-14 of 8000 years and a stable world population of 2×10^9 are assumed. The genetic effects estimated for the carbon-14 radiation dose are doubled to take into approximate account the transmutation effect, as discussed earlier. Depending in part upon whether absolute numbers or fractional increases are considered, different persons may place different interpretations upon the figures given in Table 4. Furthermore, individuals differ in their viewpoints regarding the genetic effects in the next few generations as opposed to effects over the next 8000 years.

Leipunsky (3) has published estimates of the genetic and leukemogenic hazards of nuclear weapons. As noted earlier, he assumed a very high neutron escape per 200 Mev of energy released—a figure that may be high by a factor of 4 to 6 as compared with actual neutron escape from U.S. weapons. Except for the fact that he ignores the transmutation effect of carbon-14, his calculations of the genetic hazards appear to be valid for the doses he assumed, although he made computations for only the gross physical or mental defect category. There also appear to be errors in Leipunsky's calculation of the leukemogenic hazards—a calculation based on the as yet unproved linear relationship between dose and leukemia incidence postulated by Lewis (19). Since leukemia resulting from strontium-90 (the major fission product contributing to the bone dose) would be largely of bone-marrow origin, Leipunsky's use of Lewis' (19) values for probability of leukemia from bone-marrow and lymphatic-system irradiation resulted in estimates twice those obtained when the appropriate value for the probability as given by Lewis is employed. Finally, Leipunsky's calculation of both the bone and gonadal doses may be questioned because of his assumption

that the internal cesium-137 dose is proportional to cumulative, rather than annual, deposition of fallout and by his consideration of cesium-137 as the only contributor of external gamma radiation. Except for these differences in assumptions affecting the estimates of dosages, including assumptions about the number of neutrons escaping to air, we are in general agreement with Leipunsky's calculations.

Conclusions

1) Subject to large uncertainty, the transmutation effect of carbon-14 atoms contained in the genetic material of the human body could lead to about the same number of genetic mutations as the radiation effect from carbon-14.

2) Genetic damage estimates are subject to large uncertainties and should be used in this light.

3) Because nuclear weapon detonations have already produced radioactive carbon-14, the number of persons in the world likely to have genetic or other abnormalities from carbon-14 radiation will be increased. Expressed as a fraction, the increase from bomb testing to date is very small, but the total number of persons likely to be affected in the next 8000 to 10,000 years may not be considered small by some persons.

References and Notes

1. E. C. Anderson, *Ann. Rev. Nuclear Sci.* 2, 63 (1953).
2. J. N. Davidson, *The Biochemistry of the Nucleic Acids* (Wiley, New York, 1950).
3. O. I. Leipunsky, "The radiation hazards of ordinary explosions of pure hydrogen and ordinary atomic bombs," *Atomnaya Energ.* 3, 530 (1957). This was also available to us in translation through the United Nations.
4. W. F. Libby, paper presented before the Swiss Academy of Medicine, Lausanne, Switzerland, 27 Mar. 1958 (1958), p. 24.
5. B. S. Strauss, *Radiation Research* 8, 234 (1958).
6. H. A. McQuade, M. Friedkin, A. A. Atchison, *Exptl. Cell Research* 11, 249 (1956).
7. J. F. Crow, *Rept. of the Congress of the*

- United States, Joint Committee on Atomic Energy, Special Subcommittee on Radiation: Hearings on the Nature of Radioactive Fallout and its Effect on Man* (Government Printing Office, Washington, D.C., 1957).
8. T. C. Carter, *Proc. Roy. Soc. London B147*, 402 (1957).
 9. "The Biological Effects of Radiation," *Natl. Acad. Sci.-Natl. Research Council Publ.* (1956).
 10. "The Hazards to Man of Nuclear and Allied Radiations," *Med. Research Council (Brit.) Spec. Rept.* (1956).
 11. "Effect of Radiation on Human Heredity," *World Health Organization Rept.* (1957).
 12. "On the Effects of Atomic Radiation," *U.N. Scientific Subcommittee Publ.* (United Nations, N.Y., in press).
 13. N. E. Morton, J. F. Crow, H. J. Muller, *Proc. Natl. Acad. Sci. U.S.A.* 42, 855 (1956).
 14. W. L. Russell, "Genetic effects of radiation in mice and their bearing on the estimation of human hazards," in *Peaceful Uses of Atomic Energy* (United Nations, N.Y., 1956), vol. 11, pp. 382-383.
 15. J. R. Arnold and E. C. Anderson, *Tellus* 9, 28 (1957).
 16. W. F. Libby, *Science* 122, 57 (1955).
 17. —, "The radioactive fallout and radioactive strontium," paper presented at Northwestern University, Evanston, Ill., 19 Jan. 1956.
 18. —, "Carbon-14 from bomb tests," statement delivered before the Federation of American Scientists, Washington, D.C., 1 May 1958.
 19. E. B. Lewis, *Science* 125, 965 (1957).

News of Science

De Hevesy to Receive \$75,000 Atoms for Peace Award

George Charles De Hevesy of the Research Institute for Organic Chemistry, Stockholm, Sweden, has been named winner of the second \$75,000 Atoms for Peace Award for his discovery and development of tracer techniques in chemistry, biology, and medicine. The Hungarian-born chemist and teacher, who received the Nobel Prize in 1943, was selected unanimously from a list of 111 nominees representing 19 countries throughout the world. De Hevesy will attend presentation ceremonies in New York City in January 1959.

The award was announced by Detlev W. Bronk, president of the Rockefeller Institute and the National Academy of Sciences, and chairman of the Board of Trustees of Atoms for Peace Awards. In tribute to De Hevesy, Bronk said:

"His willingness to accept a failure in a chemical experiment as a starting point for new explorations led to the first use of radioactive isotopes as tracers in chemical studies. His application of

this discovery to biological systems has revolutionized our concept of the biochemical processes in living organisms.

"He was the first to apply both natural and artificial isotopes to the study of plants and animals; he introduced the use of stable isotopes and he was the first to explore the possibility of creating radioactive substances within the system being studied by means of neutron bombardment.

"These discoveries, now adopted in laboratories and hospitals all over the world, are certainly among the most important advances in the peaceful use of atomic energy in our time. In the fields of chemistry, biology, geology, and medical research and therapy, the results of De Hevesy's contributions are continually being extended and widely utilized.

"His own work has continued undiminished and the output of scientific papers from his laboratory in Stockholm is both copious and significant."

Born in Budapest in 1885, De Hevesy took his doctorate at Freiburg in 1908. After a period of study in Switzerland and Germany, he went in 1911 to work

with Ernest Rutherford in England. Here he failed to separate radium D from lead. This failure resulted in De Hevesy's development of the use of the radioactive element (now known to be an isotope of lead and not readily separable from it by chemical means) as a tracer for lead, first reported in 1912.

From 1913 to 1920, at the University of Budapest, first as a lecturer, then as professor of physical chemistry, De Hevesy continued his studies of lead in organic and inorganic compounds using the tracer technique. In 1920 he joined the Institute for Theoretical Physics in Copenhagen. Here, with the physicist D. Coster, he discovered the chemical element hafnium.

In 1933 he applied the tracer technique to the study of chemical processes in plants. This was the first use of the technique in living systems. As new potential isotope tracers became available, De Hevesy extended his techniques to include the use of heavy water in 1934 and of artificially radioactive elements in 1935.

He also pioneered the activation of radioactive compounds within the system being studied by means of neutron bombardment.

Since the second World War, De Hevesy has worked both in Copenhagen and Stockholm. His publications since 1950 include more than 50 papers. He is author or coauthor of four texts on radioactivity and its uses in chemistry, biology, and medicine.

The Atoms for Peace Award was created as a memorial to Henry Ford and



George Charles De Hevesy

his son, Edsel Ford, in response to President Eisenhower's appeal at Geneva for international efforts to develop nuclear energy for peaceful purposes. The Ford Motor Company has set aside \$1 million for the awards, the first of which was presented to Niels Bohr on 24 October 1957.

The awards are administered by a Board of Trustees, which with the assistance of an Advisory Committee on Nominations, selects the annual winner "without regard for nationality, politics, or any other consideration except the merit of the contribution." Trustees of the award, in addition to Bronk, are Ralph J. Bunche, Arthur H. Compton, Mildred McA. Horton, James R. Killian, Jr. (inactive), and Alan T. Waterman. The Advisory Committee on Nominations for the 1958 Award were Robert A. Lovett, Robert F. Bacher, Robert F. Loeb, Robert E. Marshak, and Charles A. Thomas.

FAS Urges Permanent Cessation of Nuclear Tests

The Council of the Federation of American Scientists, at a meeting in New York on 23 November, released a statement urging the permanent cessation of nuclear tests. The federation now has a membership of approximately 2200 scientists and engineers of all fields. Its Executive Committee this year includes: chairman, Augustus H. Fox, professor of mathematics, Union College (Schenectady, N.Y.); vice chairman, Walter Selove, professor of physics, University of Pennsylvania; secretary, Harry Palevsky, physicist, Brookhaven National Laboratory; treasurer, Leonard Herzenberg, biochemist, National Institutes of Health; Paul M. Doty, professor of chemistry, Harvard University; and

Frank Ham, physicist, General Electric Research Laboratory. The FAS statement follows.

"Recent calculations, based on official information, indicate that there are probably enough large nuclear bombs in present stockpiles to destroy the human race. This could be accomplished by the blanket of radioactive material which could be laid down by the explosion of a massive number of nuclear bombs. For example, if even a fraction of present stockpiles were exploded on the territory of even a large country, a deposit of radioactive material would be produced of such intensity that all life in the open would be destroyed, and life would not be possible on the surface of the earth until about one to three years had passed.

"It would furthermore be possible for a fanatical ruler to pull down the entire human race to destruction. With a stockpile of the size that now exists, it is possible to cover the entire earth with a radiation level which for ten years would remain sufficiently intense to prove fatal to all living beings on land. This could be brought about by a decision of a small number of people.

"The argument has been advanced that continued testing is important to develop defensive weapons that would be effective in providing protection. But expert opinion has been given to the effect that there is not, and very likely never will be, any meaningful defense against massive attack. It may be possible to inflict destruction on an opponent, but no nation can any longer give protection and security to its own people. Only a 100 percent defense can prevent annihilation, and 100 percent defense can never be expected, especially in the first stage of an intensive attack.

"We have thus come to a new period in history, in which the human race can destroy itself. The new weapons of mass destruction are too dangerous to be left under sovereign national control. In these circumstances our primary goal must be to bring these weapons under international control. A universal test cessation, under international inspection, offers promise of being the most practicable first step toward international control of mass destruction weapons.

"Although it is the responsibility of the military to seek further development of weapons of all types, it must be stressed that security is not available through military means. Therefore an objective of moving toward effective disarmament must come before considerations of technical improvements which further testing might produce in nuclear weapons.

"We urge that the parties negotiating on a test cessation agreement nor stand on any narrow position which will impede an agreement leading toward the

major goal. The negotiators must adopt all reasonable measures which will provide satisfactory assurance to all parties that no further significant nuclear weapons development will occur.

"An acceptable agreement must include the immediate establishment of an effective test detection system, which the experts' conference reported to be technically feasible. As to the initial period of test cessation, we should agree to a permanent ban, subject only to the condition that the detection system be put into operation within an agreed period. Certainly any cessation period limited in duration must be longer than the period required merely to prepare another series of test explosions. The people of all countries may rightly demand that the governments of all nuclear powers show clearly that they sincerely desire to end the testing of nuclear weapons."

Research Advisory Service

The National Science Foundation has announced the establishment of a Research Information Center and Advisory Service on Information Processing to be operated jointly by the foundation and the National Bureau of Standards. The new service is designed to bring together research and development data on methods and equipment for the automatic processing of scientific information. It is further designed to foster closer cooperation among groups in industry, private foundations, universities, professional societies, and the Federal Government concerned with developing and improving methods of rapid and efficient handling of large volumes of information.

Initiation of the service is a part of a broad program being developed by the National Science Foundation to improve the quality of scientific information services and shorten the time spent by scientists in searching the literature. Other phases of the broad program include the support of scientific publications, translations of foreign scientific literature, and support of information and data-processing centers.

The foundation has made a grant of \$105,000 to the National Bureau of Standards for the establishment and first year's operation of the service, and will establish policies for its use. The service will be staffed by NBS personnel, who will analyze materials received and furnish requested technical advice. The Council on Library Resources has contributed \$20,000 toward operating costs during the first 2 years. The council, which supports research on library problems, was established in 1956 with the Ford Foundation's financial support.

During the first 6-9 months, the serv-

ice will assemble and organize research and development data on methods and equipment for the automatic processing of information expressed in words, diagrams, or other non-numerical forms. Continuing tasks, to be begun as rapidly as possible, will be as follows.

1. Explore known sources and locate undeveloped sources of information on current research and development activities.

2. Establish and maintain a central reference file of information on current projects, researchers, and publications in the field. Descriptive information on work in progress will continue to be published in the foundation's semiannual report on *Current Research and Development in Scientific Documentation*.

3. Follow developments closely, analyze collected information, and from time to time prepare and publish reviews of progress.

4. Test and compare various procedures and techniques for the manipulation or searching of information.

5. Provide federal agencies and cooperating private organizations with requested technical advice on information-processing problems and on proposed research in the field. The service will not undertake to evaluate research proposals, but will furnish advice on the relation of proposed programs of research to other activities in progress and will suggest specialists believed to be particularly well-qualified to evaluate proposed research.

Eventually, it is hoped the service will be able to provide cooperating private organizations and federal agencies with consulting services regarding the use of machines as aids in research on information processing, the availability of machine facilities for testing theories and techniques, and the availability for research purposes of texts and other source data in a form suitable for machine processing.

Organizations and individuals engaged in research and development activities or planning programs in these areas may request further information about the new service and the procedures to be followed in requesting advice or information by writing to the Research Information Center and Advisory Service on Information Processing, Program for Documentation Research, National Science Foundation, Washington 25, D.C.

Illinois Radio Telescope

A radio telescope with a larger receiving area than that of any similar existing instrument will be constructed by the University of Illinois. University trustees have recently approved purchase of a 220-acre site near Union Corner, Ill., 35 miles east of the Urbana-Cham-

paign campus. In the area, on the northeast bluff of the Vermilion River, is a ravine in which the university will build a trough-shaped reflector that will be 600 feet long, north and south. The trough will be 400 feet wide and 65 feet deep. The facility is being financed by a \$233,000 grant from the Navy.

The new instrument, which will be similar in design to the other large radio telescopes being considered in England, Australia, and the United States, will have 160,000 square feet of receiving area. This is from two to three times more receiving area than the radio telescope now in use at Manchester, England. However, unlike the British instrument, the Illinois telescope will not be steerable. Observers using it will have to wait until the object they want to examine is brought over the telescope once a day as the earth rotates on its axis. A fairly large area of the sky will be observable.

WHO Procedural Guide

A guide to procedures and practices of the World Health Organization, Geneva, Switzerland, will be compiled during the next 3 years with the aid of a \$25,000 grant from the Rockefeller Foundation. The guide will cover both the internal administration of WHO and its political and program relationships with the member governments of the United Nations. In addition, the "repertory of practice" will include the historical aspects of the development of international health activities and of the establishment of WHO.

The repertory of practice is needed to preserve in factual form the current practices of WHO and to serve as a basis for operation and understanding. The document will be valuable not only to WHO and the UN but also to health agencies throughout the world in formulating programs and policies relating to WHO.

Planet Earth

A new teaching aid designed to help stimulate science interest in the schools was announced recently by the National Academy of Sciences. Known as "Planet Earth," the new aid covers the scientific fields studied during the International Geophysical Year. It has three major components. The first includes six large, full-color posters entitled "The Earth," "The Oceans," "The Poles," "Sun and Earth," "Weather and Climate," and "Space."

The second component is a profusely illustrated 44-page student brochure that reproduces the posters and describes the work of scientists in a dozen or more

fields. The third component is a teacher's kit containing suggestions for classroom experiments, background material on aspects of the IGY and the earth sciences, a description of teaching methods related to the IGY in the Baltimore County schools, a list of scholarships available to students in the field of science, and other materials.

"Planet Earth" was prepared under the direction of Hugh Odishaw, executive director of the United States National Committee for IGY. A ten-member advisory committee that included AAAS education director John R. Mayor assisted in shaping the project. Financial support was provided by the National Science Foundation and the Ford Foundation. The academy was also guided in the early stages of the project by advice and assistance from Ellsworth Obourn, U.S. Office of Education; Robert Carleton, executive secretary, National Science Teachers Association; and officials of the National Science Foundation. The final materials were reviewed by scientists engaged in the US-IGY program.

After a year in preparation, "Planet Earth" is now ready for distribution to the schools. The package and its components are priced at cost. A classroom package—6 posters, 30 student brochures, and a teacher's kit—is priced at \$9.50. Distribution is through the National Academy of Sciences Publications Office, Washington, D.C.

Waste Disposal

The University of California at Berkeley will host the first International Conference on Waste Disposal in the Marine Environment during the summer of 1959. The 3-day meeting will provide a forum for the international exchange of knowledge among scientists and engineers of many disciplines, interests, and organizations who are concerned with marine pollution research throughout the world. A tentative agenda lists as discussion topics (i) Waste Disposal, (ii) Public Health, (iii) Nearshore Oceanography, (iv) Receiving Water Analysis, (v) Marine Biota, and (vi) Estuarine Hydrography.

The program is presented by the U.C. Sanitary Engineering Research Laboratory, the Institute of Marine Resources, and University Extension in cooperation with the California State Water Pollution Control Board. Conference chairman is Erman A. Pearson, associate professor of sanitary engineering at the university and chairman of the Research Consulting Board of the State Water Pollution Control Board.

This conference will provide the first opportunity for an international exchange of information on marine waste

disposal. Although a great deal of industrial and municipal waste is discharged into the marine environment, research in this area has been largely neglected as compared to research on the fresh water environment. Further information about the program may be obtained from the Department of Conferences, University Extension, University of California, Berkeley 4, Calif.

News Briefs

The second program of the season in the "Conquest" television series, which will be devoted partly to cancer research and partly to the study of volcanoes, will be shown on 14 December at 5 P.M. (E.S.T.) on the CBS Television Network. Participating in the report on cancer research will be C. P. Rhoads, director of the Sloan-Kettering Institute for Cancer Research in New York. In the latter half of the program, the audience will be shown an active volcano—Kilauea in the Hawaiian Islands. Two volcanologists will participate: Gordon MacDonald, a geologist at the University of Hawaii, and Jerry Eaton, director of the Hawaiian Volcano Observatory at Kilauea. "Conquest" is presented in cooperation with the AAAS and the National Academy of Sciences, under the sponsorship of the Monsanto Chemical Company.

* * *

The School of Allied Medical Professions of the University of Pennsylvania formally dedicated its new quarters at 39th and Pine Streets, Philadelphia, on 25 November. The completely renovated spacious old building makes it possible for the various academic programs of the school to be housed under one roof. These programs include physical therapy, occupational therapy, medical technology, and oral hygiene.

* * *

The American Association of Poison Control Centers was formed in Chicago on 21 October 1958. Officers elected are as follows: president, Robert Grayson, organizer of the poison control center at Jackson Memorial Hospital, University of Miami School of Medicine; vice president, William C. Adams, University of Louisville School of Medicine; and secretary-treasurer, Harry Raybin, New York City Department of Health.

Membership is open to both individuals and organizations. The new association hopes to stimulate educational programs and scientific research on toxic substances; assist state and local officials and voluntary agencies in the field of poison control; set up standards for operation of poison control centers; provide information to the public and develop information services; and help develop insurance liability programs.

The Boston Psychoanalytic Society and Institute celebrated its 25th anniversary on 30 November. The theme of a special meeting, attended by some 600 people, was the creative role played by Boston psychoanalysts in the development in the United States of their specialty. The Society and Institute, which was formally organized in 1933, is the outgrowth of the early interest in the work of Sigmund Freud aroused among Boston physicians. James J. Putnam, first president of the American Neurological Association (1911) and first professor of neuropathology at Harvard, was a pioneer and was identified by Freud as "the first psychoanalyst in America." The original Boston Psychoanalytic Society, which was reorganized in 1933, was established in 1928 with Isador Goriat as the first president.

* * *

The following chemicals are wanted by the National Registry of Rare Chemicals, Armour Research Foundation of Illinois Institute of Technology, 13 W. 33 St., Chicago 16, Ill.:

4-amino-3,5-dimethylbenzoic acid; 1,2,3,4-benzenetetracarboxylic acid (melophanic acid); 3-bromoanisole; 3-bromopropenylbenzene; 3-bromosalicylic acid; *p*-chlorocumene; cobaltous cyanate; diallyl bicyclo-(2.2.1)-hept-5-ene-2,3-dicarboxylate; 2,6-diaminobenzoic acid; 2,4-dichloro-3-methylphenol; unsymmetrical diethyl dicyclohexyl thiuram disulfide; 1,4-dihydronaphthalene; 5,5-dimethylheptene-3; N-ethylallylamine; ethyl phosphine; hexakis(hydroxymethyl) melamine; N-hexanal; N-hexyl azide; lithium cyanide, anhydrous, and 4-trimethylsilylbenzoic acid.

* * *

Contracting procedures of the National Aeronautics and Space Administration will conform in every practicable way to the Armed Services Procurement Regulations. This decision should be welcomed by potential NASA contractors, since industry has become quite familiar with the ASPR in the past 10 years. It will not be necessary to learn how to operate under widely divergent NASA regulations.

Scientists in the News

WALLACE R. BRODE, president of the AAAS and science adviser to the Secretary of State, was awarded the Medal for Distinguished Work in Spectroscopy of the Society of Applied Spectroscopy at the society's annual meeting in New York on 6 November.

HERMANN I. SCHLESINGER, professor emeritus of chemistry at the University of Chicago, has been named winner of the 1959 Willard Gibbs Medal of the Chicago Section of the American

Chemical Society. The medal will be awarded on 22 May 1959 at a dinner in the Furniture Club, Chicago. Schlesinger achieved fame for his basic research in the compounds of boron. The results of his scientific inquiries led to such far-ranging applications as rocket fuels and vitamin manufacture.

PAUL E. KLOPSTEG, AAAS president-elect, is the new chairman of the National Academy of Sciences-National Research Council's Committee on Atmospheric Sciences. He succeeds LLOYD V. BERKNER, president of Associated Universities, Inc., who resigned in order to devote his full energies to his new position as chairman of the Academy-Research Council's Space Science Board.

Since assuming the committee chairmanship, Klopsteg has retired from his position as associate director (research) of the National Science Foundation, with which he has been associated since 1951. Upon his retirement, Klopsteg was named special consultant to the NSF director for a period of a year.

The Committee on Atmospheric Sciences (originally the "Committee on Meteorology") was organized by the NAS in April 1956 for the purpose of bringing together scientists from meteorology and related physical and geophysical fields to view in broad perspective the present position and future requirements of meteorological research and to recommend the general outline of a program which would accelerate progress in this important field. In January 1958, an "interim report" of the committee offered a series of recommendations in pursuance of its goals. These included the granting of Federal funds to increase support for meteorological research in universities, the establishment of a National Institute of Atmospheric Research, and the creation of more promising career opportunities for young meteorologists.

I. S. RAVDIN, vice president for medical development, University of Pennsylvania, and professor of surgery, has received the first annual Lovelace Foundation Award. President Eisenhower sent a congratulatory telegram to Ravdin at the presentation ceremony in Albuquerque, N.M., where the foundation has headquarters.

Lt. Commander JOHN H. EBERSOLE, U.S. Navy, medical officer of the U.S.S. *Seawolf*, one of the Nation's first atomic-powered submarines, has received the Gorgas Medal for his role in the development of nuclear medicine. The \$500 award was presented on 19 November at the annual dinner of the Association of Military Surgeons in Washington, D.C. The Gorgas Medal is sponsored by Wyeth Laboratories in memory of Sur-

geon General William C. Gorgas, whose work in controlling yellow fever made possible the construction of the Panama Canal.

BENTLEY GLASS, professor of biology at Johns Hopkins University and for some years a member of the AAAS editorial board, will discuss "Genes and the Man—New Vistas" as a Sigma Xi national lecturer at a number of colleges and universities in December and January.

McCHESNEY GOODALL, formerly of the Duke University School of Medicine, has joined the staff of the University of Tennessee Memorial Research Center as research professor and assistant director. Goodall is a neurophysiologist whose interests include space medicine.

IAN CAMPBELL, professor of geology and executive officer of the Division of Geological Sciences at the California Institute of Technology, has been named chief of the Division of Mines in California's Department of Natural Resources, effective early in January 1959.

HACK ARROE has been named head of the Physics Division in the Denver Research Institute of the University of Denver.

ARTHUR UHLIR, Jr., has joined Microwave Associates, Inc., Burlington, Mass., as director of semiconductor research and development. He was formerly a member of the technical staff of Bell Telephone Laboratories, Inc., Murray Hill, N.J.

The following mathematicians have reported new appointments for the academic year 1958-59.

C. W. CURTIS, associate professor on leave from the University of Wisconsin, has been appointed visiting associate professor at Cornell University.

R. J. DUFFIN, professor on leave from Carnegie Institute of Technology, has been appointed director of special research in applied mathematics at Duke University.

SIMON GREEN, associate professor at the University of Tulsa, has been appointed associate professor at the University of South Carolina.

J. W. HAMBLEN, assistant professor at Oklahoma State University, has been appointed director of the computing center and associate professor of statistics at the University of Kentucky.

T. E. HULL, associate professor at the University of British Columbia, has been appointed visiting associate professor at the California Institute of Technology.

D. A. KEARNS, assistant professor

at the University of Maine, has been appointed professor at Merrimack College.

O. M. KLOSE, associate professor at Seattle University, has been appointed associate professor at Humboldt State College.

JOHN KRONSBELN, professor at Evansville College, has been appointed professor at the University of Florida.

G. G. LORENTZ, professor at Wayne State University, has been appointed professor at Syracuse University.

E. P. MILES, JR., associate professor at Alabama Polytechnic Institute, has been appointed associate professor at Florida State University.

The University of Michigan has appointed ARLEN R. HELLWARTH as associate professor of engineering, effective 1 February 1959, and as secretary and assistant dean of the College of Engineering, effective 1 July 1959. He will do some teaching during the spring semester and then replace associate dean WALTER J. EMMONS, who is retiring on 30 June 1959. Since 1933, Hellwarth has been associated with the Detroit Edison Company. For ten of these years his work was concerned with engineering, planning, and operation of communication and electrical power systems. For 15 years, he served in supervisory positions and administrative work in various phases of personnel.

Also at Michigan, CHARLES G. GORDY, professor of industrial engineering, will retire as professor emeritus on 1 February 1959. He has been on the faculty of the College of Engineering since 1921. He became the first professor of industrial engineering at the university and was until recently the only one holding this title. During his 37 years of service, he has taught continuously without sabbatical leave, sick leave, or any other absence from duty.

Major General HOWARD G. BUNKER, U.S. Air Force (Ret.), has joined the staff of the Rand Corporation, Santa Monica, Calif., where he will serve as special assistant to E. J. Barlow, chief of the Engineering Division. Bunker's last military assignment was as deputy inspector general of the Air Force. Before that, for 4 years, he served as assistant for atomic energy, USAF headquarters.

EUGENE BOLLAY, meteorologist, has been appointed director of research, meteorology instrumentation, at BJ Electronics, Borg-Warner Corporation, Santa Ana, Calif. Bollay was formerly president and technical director of Northam Electronics, Inc., recently acquired by BJ Electronics. He will serve in specialized areas of instrumentation and applications, particularly as related to weather and meteorology.

Recent Deaths

PAUL O. CHATFIELD, Philadelphia, Pa.; 41; assistant professor of neurology at Jefferson Medical College; chief of the section of clinical neurophysiology at the National Institute of Neurological diseases and Blindness, Bethesda, Md., 1953-56; assistant professor of physiology at the Harvard Medical School; 1946-53; 19 Nov.

LEE M. EATON, Rochester, Minn.; professor of neurology at the Mayo Foundation; chairman of the sections of neurology at the Mayo Clinic and president of the Association for Research in Nervous and Mental Diseases; president of the Central Neuro-Psychiatric Association in 1953; 19 Nov.

WARREN W. FUREY, Chicago, Ill.; 60; clinical professor of radiology at Loyola University's Stritch School of Medicine; chief radiologist at Mercy and at Little Company of Mary Hospitals; past president of the Radiological Society of North America, and of the Chicago Medical Society; 19 Nov.

CHARLES F. KETTERING, Dayton, Ohio; 82; mechanical engineer whose most important inventions are the automobile self-starter and the two-cycle diesel engine; retired in 1948 as vice president of the General Motors Corporation and director of the General Motors Research Laboratories; AAAS President, 1945; chairman of the National Inventors Council since 1940; chairman of Charles F. Kettering Inc., and vice president of the Charles F. Kettering Foundation, which he founded in 1925 at Antioch College; director of the National Cash Register Company at Dayton, for which he developed the first electric cash register, and director and first president of the Ethyl Corporation; 25 Nov.

WILLIAM H. LEAK, West Stamford, Conn.; 78; New York dentist, who in 1943 was named the first curator of Columbia University's Museum of the School of Dental and Oral Surgery; head of the Post-Graduate Dental Clinic of Columbia University; 21 Nov.

PAUL C. SQUIRES, New London, Conn.; 64; psychologist in the human engineering branch at the Navy Submarine Base; had been associate professor of psychology at the University of Vermont and assistant professor at the University of Kansas; taught at Sampson College (N.Y.) and at the University of Rochester; 25 Nov.

FRANK A. WATERMAN, Northampton, Mass.; 93; retired professor of physics, Smith College, where he taught from 1897 to 1933; taught at Purdue University and at Princeton before joining Smith; for many years chief examiner and chief reader in physics in the College Entrance Examination Board; designed apparatus for use in elementary physics laboratories; 17 Nov.

Book Reviews

Comparison of the Large-Scale Structures of the Galactic System with that of Other Stellar Systems. International Astronomical Union Symposium No. 5. Held in Dublin, 2 September 1955. N. G. Roman, Ed. Cambridge University Press, New York, 1958. 72 pp. + plates. \$3.

Nineteen workers in the general field of galactic structure give, in this thin volume, abstracts of papers they presented at a symposium in Dublin in 1955 on the occasion of a meeting of the International Astronomical Union. The volume is valuable as a record of progress in the study of galaxies, especially of our own. It will not be so valuable to the general reader in search of final answers because the subject is now in agitated flux. Radio astronomy has entered the field. Neutral hydrogen radiation from interstellar space has opened new chapters in the astronomer's "Book of Knowledge" of matters cosmic. The Cepheid variables and the high-luminosity blue stars have to some extent betrayed us and made a confusion of the extragalactic distance scale. The universe expands at a lesser speed than we thought a decade ago, and therefore the age of the expansion and the speed of the evolution of galaxies and stars is under revision.

In the face of these semichaotic conditions, the astronomers from five countries have, in the symposium under review, clearly pointed the way to a better understanding.

Unfortunately, Walter Baade's excellent interim report on the structure of the Great Andromeda galaxy is made nearly useless by the omission from the book of the revealing photographs made by him with the giant reflectors in California. The reports on radio astronomy by the Dutch and English astronomers, however, are full of good results and speculations, and one can see that the greater radio equipment of the near future will revise numerous conclusions, answer many questions, and ask still more. The contributions from the Soviet writers are outstanding in special subjects: Kukarkin on the use of variable stars for the analyzing of galactic structure; the late G. A. Shajn on the short durations of diffuse nebulae; and Am-

bartsumian on the possible existence of scattering "associations" of galaxies, analogous to the scattering associations of stars which he has discovered and explored.

One of the Soviet writers (Vorontsov-Velyaminov) is a strong dissident, openly challenging the conclusions of practically everybody. Although he was not a participant in the symposium, his paper was included in the volume at the special request of the Russian leader, Kukarkin.

One result has clearly emerged from the conference and its book-length report; it is that both the structure of our galaxy and the evolution of all galaxies are more complicated than we thought in the simple days of ten years ago.

HARLOW SHAPLEY

*Harvard College Observatory,
Harvard University*

Physical Geology. L. Don Leet and Sheldon Judson. Prentice-Hall, Englewood Cliffs, New Jersey, ed. 2, 1958. ix+502 pp. Illus. \$7.50.

Four years ago, after publication of a review commending the inclusion, in the first edition of this text, of some elementary chemistry and atomic theory as background for an understanding of geology, I was mildly dumbfounded by one professor who wrote, "The book contains too much on atomic structure . . . we fear that these pages would floor the student and he would never see the next chapter."

Thus one teacher's respected text may be another's doorstep. But those who wish to introduce into elementary geology courses some background information in fundamental principles from related sciences will find that this book employs the approach introduced in the first edition, refined and sharpened by several years of practical use in hundreds of classrooms throughout the country.

The organization of chapters is changed and improved. "Minerals" and "Igneous rocks" are now considered separately near the beginning of the book; they are followed immediately by a discussion of "Igneous activity," which formerly was rather illogically lumped with "Metamorphism" near the end of the text.

"Geologic time" is removed from the appendix, expanded considerably, and given separate chapter rank. The discussion of wind action now appears in a chapter headed "Deserts," though some of the activity described does not occur under desert conditions. "Lakes and swamps" have a chapter of their own instead of being immersed in "Running water," "Underground water," and "Glaciation"; all of these chapters remain otherwise not greatly altered. "Earthquakes" and "The earth's interior," specialties of the senior author, now are separated and splendidly presented in relatively compact form. Several new diagrams on "Rock-deformation and mountain-building" clarify the presentation of this complex subject. The final chapter on "Useful materials and energy" is greatly expanded and offers much up-to-date information in this fast-changing field.

Many portions of the book have been rewritten, and new illustrations and diagrams have been added. The approach is stimulating and rigorous. Geology is presented as an exact science, drawing support from mathematics, physics, chemistry, and other disciplines, but still finding uncertainties on its own doorstep. For example, in the discussion of exfoliation we read, "How these slabs of rock come into being in the first place is still a matter of dispute," or in the section on feldspars, "Mineralogists still do not understand the precise process by which the feldspars weather." Here is refreshing departure from the practice of pretending in an elementary text that all answers in the science are known.

Unfortunately, few direct references are made to controversial views in ways which will enable the curious student readily to seek additional information. For instance, although Johnson's and Shepard's classifications of ocean shorelines are briefly summarized, neither authority is cited by name. Only one reference to the subject is given at the chapter's end, and that not in a way which shows the student that it has any connection with the controversial views previously discussed.

Considerable reference material is included at the end of the book. A 27-page glossary covers most of the technical terms used in the text. There also are appendices on the chemical elements, on mathematical exponents and their use in expressing distances and sizes, on minerals and their characteristics, and on topographic and geologic maps.

In all, the book provides a sound elementary foundation in geology for serious and competent nonmajors, as well as for students who plan further work in the science.

HALL TAYLOR

*Department of Geology,
Columbia University*

Current Trends in the Description and Analysis of Behavior. Nine lectures under the auspices of the Department of Psychology in the College of the University of Pittsburgh delivered during March 11-12, 1955, and March 8-9, 1956, in the Stephen Foster Memorial Auditorium. Robert Glaser and others. University of Pittsburgh Press, Pittsburgh, 1958. 242 pp. \$4.

This is a set of lectures by research experts in fields ranging from physiological psychology to psychoanalysis. The lecturer was asked to talk about research trends and probable future developments, particularly in methodology. The choice of subject matter was dictated by "the general problem of measurement since there is the continuous need for the development of methods to quantify the stubborn and elusive phenomena of behavior."

Glaser sees the social psychologists becoming more interested in the formal or task-oriented group. Zubin wants models rather than more facts in psychopathology. Lindsley describes the reticular activating system of the brain and his recent work on the neurophysiology of perception. Nowlis describes recent investigations on communication, persuasion, and mood. Cofer offers a theoretical discussion of processes that mediate between stimulus and response. Guetzkow describes the interaction between methods and models in social psychology. Carroll examines linguistic coding as an approach to the field of cognition. Hamlin perceives a trend in the direction of more complete observation of behavior in psychotherapy, and French analyses the reactive motives of guilt and shame.

JOHN L. KENNEDY
Department of Psychology,
Princeton University

Spot Tests in Inorganic Analysis. Fritz Feigl. Translated by Ralph E. Oesper. Elsevier, Amsterdam, ed. 5, 1958 (order from Van Nostrand, Princeton, N.J.). 640 pp. Illus. \$13.25.

This is the fifth edition of a book which in its fourth (1954) edition had the title *Spot Tests* [vol. I]: *Inorganic Applications*; that edition, in turn, was an enlargement of the "inorganic" portion of *Qualitative Analysis by Spot Tests, Inorganic and Organic Applications* (1946, 1939, and 1937). The present edition, with its addition of numerous new tests, improvement of old ones, and inclusion of new techniques, continues to hold its place as the authoritative work by the outstanding leader in the field of spot testing. Ralph Oesper's translation is excellent.

The total number of tests and applications has grown from 451 in the fourth edition to 561 in the present one. New tests are given for aluminum, calcium, cobalt, lithium, molybdenum, palladium, potassium, tin, titanium, tungsten, and uranium as cations or metalloanions. Acids included for the first time are aminosulfonic (sulfamic), cyanic, the hypohalogenous acids, hyposulfurous (dithionous), and perchloric. Among the new techniques is the ring oven method according to Weisz. Twenty-seven of the 95 sections in chapter 7, on "Applications of spot reactions in tests of purity examination of technical materials, studies of minerals," are new.

A tabular summary of the limits of identification attained by spot tests, along with cross references to each test and an extensive subject index, add to the usefulness of the book. It is a volume that few analytical chemists can afford to be without.

EDWARD L. HAENISCH
National Science Foundation

Advances in Veterinary Science. vol. 4. C. A. Brandly and E. L. Jungherr, Eds. Academic Press, New York, 1958. xi + 414 pp. \$12.

Of all the books published, those reporting on progress in any field of pure or applied sciences seem to me the most interesting and most useful ones. This is due to the disturbing fact that it has become impossible for anyone in any profession to keep up with the multitude of original and review articles and books published every month. The researcher as well as the ambitious practitioner must glance through hundreds of these publications before he finds the very few which are of real value to him.

Capable editors of reports such as those in this volume can render a tremendous service to those who do not have the time or, perhaps, the patience required to read all there is to be read in their particular field of interest. Brandly and Jungherr, in cooperation with a group of well-known authorities, have succeeded in surveying the true advances made in selected fields of veterinary medicine. These surveys should prove useful not only to veterinarians but also to physicians, pharmaceutical chemists, and public health officers, as the following brief description of the book's contents shows.

Frank A. Todd (U.S. Department of Agriculture) discusses the defense against imported animal diseases (pages 1-50), with emphasis on the necessary control measures taken at present to prevent the transmission to this country of many of the endemically and sporadically appearing diseases from various other parts of

the world. Bernard F. Trum and John H. Rust (Armed Forces Institute of Pathology) report (pages 51-95) on radiation injury, a most timely topic; they state that hematopoietic and germinal tissues are most radiosensitive; next in order are bones and glandular tissues; least sensitive are muscles and nerves. The contribution of A. Pommer (Vienna) concerns X-ray therapy in all its aspects, with indications for use in the treatment of numerous animal diseases (pages 98-136). Clyde Stormont (University of California) deals with genetics of lethal and semilethal traits and also with the possibilities of developing disease-resistant lines in animals (pages 137-162).

Of special interest to the practicing veterinarian are the three surveys (pages 164-263) concerning the current status of prevention and treatment of diseases affecting sheep (by Hadleigh Marsh) and swine (by Ronald Gwatkin, Ottawa, and A. Hjärre, Stockholm). The toxicity of insecticides and herbicides to livestock (pages 265-276) is creating many problems; these are treated concisely by R. D. Radeleff (U.S. Department of Agriculture). The discussion of the epizootiology of leptospirosis, by J. van der Hoeden (Ness-Ziona), is a most readable contribution by an Israeli researcher who specializes in the investigation of this relatively new animal disease (pages 277-339). And an English investigator, Norman H. Hole (Weybridge), has as his subject John's disease, which appears to be a problem of ever-increasing importance to the health of the ruminants throughout the world (pages 341-387).

Each chapter contains pages of literature references; in addition, there are an extensive author index (17 pages) and a subject index.

RUDOLPH SEIDEN
Haver-Lockhart Laboratories,
Kansas City, Missouri

A Course in Modern Linguistics. Charles F. Hockett. Macmillan, New York, 1958. xi + 621 pp. Illus. \$6.25.

The importance of this book can perhaps best be appreciated by the frequency with which it will be compared to what has been up till now the "bible" of American linguistics—Leonard Bloomfield's *Language*, published in 1933. Bloomfield's influence on Hockett is so apparent that there is little point in trying to distinguish any major differences in approach between the two. On the other hand, too much has happened in the last 25 years for Hockett's book to be considered merely a restatement of an earlier position, although it is clearly in the same tradition.

The book "is intended for those col-

lege students who take an introductory course in linguistics," and in keeping with this general purpose many, but not all, of the controversies in modern linguistics have been avoided. A wide range of topics is adequately covered; the only omission of any consequence is the lack of a cohesive chapter on semantics. In Hockett's view, semantics and phonetics are peripheral to the central grammatical, phonological, and morphophonemic systems. The grammatical system comprises an inventory of meaningful units (like the *boy-s walk-ed* in *boys walked*) and the arrangements in which they occur; the phonological system comprises the inventory of contrasting sounds (like the /bojz/ in *boys*) and the arrangements in which they occur; and the morphophonemic system is the code of correspondence rules between the grammatical and phonological systems (like the rules by which the plural -s is represented by /z/ in *boys* but by /s/ in *cats*).

In addition to discussions of these areas, with examples from a variety of languages as well as detailed analyses of English, Hockett includes presentations of language acquisition and change, the relationship of speech to writing, the esthetic use of language, and so forth. The final chapter on "Man's place in nature" is a particularly clear characterization of the differences between human language and other systems of communication, which, together with the short introductory chapter on the relationship between linguistics and other disciplines, will prove of most interest and benefit to nonlinguists.

In spite of whatever objections may be raised, this textbook will surely prove to be an excellent introduction for the next generation of students of linguistics and will probably be more widely used as such than Bloomfield's book. However, if, by virtue of this success, Hockett somehow becomes larger than Bloomfield, it is only because he is able to sit on Bloomfield's shoulders.

SOL SAPORTA

Indiana University

Farbenbestimmung in der Biologie. Parts I-VIII. Jiri Paclt. Fischer, Jena, Germany, 1958. 76 pp. Illus.

Paclt, one of the most famous biologists in Czechoslovakia, gives in this small book a general review of the technology and terminology of the colors used in the biological sciences, with the intention of forming an international basis for the terminology of colors based on a system of comparison.

The first chapter deals with the possibility of color distinction and points out that, of the effectively existing colors, only a relatively small part can be differentiated.

In subsequent chapters the author demonstrates that a decimal system for the determination of colors is the most useful one, and he compares this decimal system, based on the studies of Pavlovsky, with the older systems used generally today. He gives the general and theoretical background on which a colorimetric system can be built up. The conclusion is that only a comparative system seems to be useful for biological purposes.

After a discussion of the history of the terminology of colors, the author tries to provide an international system, because no one system existing today is entirely adequate. The existing systems—especially the Munsell System, the Horticultural Colour Chart (of the British Colour Council), the Répertoire de Couleur (of Oberthür and Dauthenay), and the Code Universel des Couleurs (of Séguéy)—still have to be used, preferably in combination.

The most useful part for English-speaking people is the dictionary of colors, in six languages—German, English, French, Italian, Russian, and Spanish. The nearly complete bibliography will enable the student to use the original literature.

This book develops nothing entirely new, but it is still useful because of the newly proposed terminology and the dictionary of colors, in six languages.

HANS PETER FUCHS

Division of Ferns,
Smithsonian Institution

Doctor Squibb. The life and times of a rugged idealist. Lawrence G. Blochman. Simon and Schuster, New York, 1958. xii + 371 pp. Illus. \$5.

The founder of the pharmaceutical house originally called "E. R. Squibb, M.D." was reared a Philadelphia Quaker. He was born in 1819 and graduated from Jefferson Medical College in 1845, during the excitement of the Mexican War. Despite the opposition of his church, which meant much to him, he acted on his grandmother Squibb's counsel—"Thee has only to decide which thee would serve—God and thy conscience or the monthly meeting"—and joined the Navy. Ten years later, after much experience at sea, followed by the almost singlehanded establishment of a drug manufacturing and control unit at the Brooklyn Navy Yard, he left to enter private business. Through the rest of his long life his all-encompassing interest was the manufacture of drugs and their honest representation. Although no longer a practicing Quaker—in fact he had been expelled for joining the Navy—he was obviously deeply concerned with commercial misrepresentation.

of drugs and devoted to drug reform. In professional societies, legislative committees, and particularly in the pages of the *U.S. Pharmacopeia*, he was a prickly protagonist for proper standards and regulations.

This story of Squibb is a well-written study of a strong and independent personality, staunch against compromise—a characteristic of many of his Victorian contemporaries. He was against sin but wanted his full interest; he worked long hours and then wrote a full diary and was impatient when his wife was frivolous; he organized his family efficiently and was hurt when his sons had minds of their own. There was more than a little of the singleminded executive type so well drawn in *The Man in the Gray Flannel Suit* in the make-up of E. R. Squibb.

WINDSOR CUTTING

Department of Medical Microbiology,
Stanford Medical School,
Stanford University

Introduction to Meteorology. Sverre Pettersen. McGraw-Hill, New York, ed. 2, 1958. x + 327 pp. Illus. \$6.75.

This book is enjoyable to read and review. It is an elementary text on a discipline that is gradually coming into its own. And Pettersen is a master in telling the story of weather problems. Yet there is no sacrifice of accuracy in order to make things easy for the student. After a first run of 17 successful years, this second edition is thoroughly revised and brought up to date. The growth in subject matter is well reflected in the 91 added pages.

The book starts with a conventional review of the general structure of the atmosphere and of weather observations. Then the author takes us to the front of scientific endeavor in his treatment of mechanisms of cloud and precipitation formation. This includes a conservative statement on the artificial stimulation of precipitation.

The facts about the various events composing the weather—showers, thunderstorms, hail, tornadoes, and so forth—are well told and illustrated. The atmospheric wind systems, the air masses and fronts carried by them, and the cyclonic and anticyclonic eddies are discussed from the vantage point of one who has made major contributions in these areas. Pettersen is an expressive spokesman in these chapters for the Norwegian school of weather analysis, in which he grew up and whose triumphs he shared.

In the remainder of the work there has been a fortunate shift of emphasis from the first to the second edition. There is less material on weather maps and

weather forecasting and more on atmospheric processes and climatology. The climatic features of the globe are described in three chapters dealing with the temperature and precipitation regimes and relating the broad scheme of geographical distribution, as represented by the Koeppen classification.

Weather problems affect all walks of life. They are important in all phases of engineering and aviation. They govern agriculture, forestry, and conservation. Students in these fields should have a meteorological course. For such purposes one could hardly find a better book than Pettersen's. Budding meteorologists, too, will find it a good mentor.

H. E. LANDSBERG

Office of Climatology,
U.S. Weather Bureau

New Books

Epilepsy. Manfred Sakel. Philosophical Library, New York, 1958. 240 pp. \$5.

The Eye. A clinical and basic science book. E. Howard Bedrossian. Thomas, Springfield, Ill., 1958. 369 pp. \$11.

Food and You. Edmund Sigurd Nasset. Barnes & Noble, New York, ed. 2, 1958. 166 pp. \$1.25.

The Graftor's Handbook. R. J. Garner. Faber and Faber, London, ed. 2, 1958. 260 pp. 25s.

Guide to the Literature of the Zoological Sciences. Roger C. Smith. Burgess, Minneapolis, Minn. ed. 5, 1958. 214 pp. \$3.50. This guide is intended to acquaint the student with some useful sources of references and to help the student become acquainted with the chief works in his specialized field and related fields. It includes information on useful and recent bibliographies, rules for making a scientific bibliography, and suggestions for the scientific writer.

Introduction to Algebraic Geometry. Serge Lang. Interscience, New York, 1958. 271 pp. \$7.25.

The Motivation, Productivity, and Satisfaction of Workers. A. Zaleznik, C. R. Christensen, F. J. Roethlisberger. Graduate School of Business Administration, Harvard Univ., Boston, 1958. 464 pp. \$6.

Phosphorus and Its Compounds. vol. I, Chemistry. John R. Van Wazer. Interscience, New York, 1958. 967 pp. \$27.50.

The Plasma in a Magnetic Field. A symposium on magnetohydrodynamics. Rolf K. M. Landshoff, Ed. Stanford Univ. Press, Stanford, Calif., 1958. 135 pp. \$4.50.

The Politics of Despair. Hadley Cantril. Basic Books, New York, 1958. 287 pp. \$5.

Principles of Statistical Techniques. A first course, from the beginnings, for schools and universities. P. G. Moore. Cambridge Univ. Press, New York, 1958. 247 pp. \$3.75.

Progress in Crystal Physics. vol. I, Thermal, Elastic and Optical Properties. R. S. Krishnan. Viswanathan, Central Art Press, Chetput, Madras 31, India. 204 pp. Rs. 20.

Psychological Stress. Psychoanalytic and behavioral studies of surgical patients. Irving L. Janis. Wiley, New York; Chapman & Hall, London, 1958. 453 pp. \$6.95.

Psychopathology. A source book. Charles F. Reed, Irving E. Alexander, Silvan S. Tomkins. Harvard Univ. Press, Cambridge, Mass., 1958. 815 pp. \$12.50.

Radioactive Isotopes in Clinical Practice. Edith H. Quimby, Sergei Feitelberg, Solomon Silver. Lea & Febiger, Philadelphia, Pa., 1958. 451 pp. \$10.

Statistics of Extremes. E. J. Gumbel. Columbia Univ. Press, New York, 1958. 395 pp. \$15.

Stoichiometry. For chemical engineers. Edwin T. Williams and R. Curtis Johnson. McGraw-Hill, New York, 1958. 363 pp. \$8.

Structural Conversions in Crystalline Systems and Their Importance for Geological Problems. Special Paper 60. Wilhelm Eitel. Geological Soc. of America, New York 27, 1958. 197 pp.

Symposium on Information Theory in Biology. Gatlinburg, Tennessee, 29-31 October 1956. Hubert P. Yockey, Robert L. Platzman, Henry Quastler, Eds. Pergamon Press, New York and London, 1958. 430 pp. \$12.

Symposium on Protein Structure. International Union of Pure and Applied Chemistry, Paris meeting, 1957. Albert Neuberger, Ed. Methuen, London; Wiley, New York, 1958. 351 pp. \$7.75. This symposium under the general chairmanship of Professor Jean Roche was attended by more than 150 protein chemists. The papers presented are divided into the following sections: "General Problems and Methods"; "Specific Proteins"; "Proteolytic Enzymes"; "Ribonuclease"; "Tobacco Mosaic Virus"; "Other Proteins and Peptides."

Theory and Methods of Scaling. Warren S. Torgerson. Wiley, New York; Chapman & Hall, London, 1958. 473 pp.

Trace Elements. Proceedings of the conference held at the Ohio Agricultural Experiment Station, Wooster, 14-16 October 1957. C. A. Lamb, O. G. Bentley, J. M. Beattie, Eds. Academic Press, New York, 1958. 422 pp. \$12. This symposium on the role of trace elements in plants, animals, and microorganisms was held as a part of the diamond jubilee celebration of the Ohio Agricultural Experiment Station.

Transactions of the Conference on the Use of Solar Energy, the Scientific Basis. vol. I, The available energy. Measurement of the radiation. 135 pp. vol. II, Thermal processes. Part I, Section A, Flat-plate collectors. 145 pp. vol. II, Section B, High-temperature solar furnaces. Solar power. 265 pp. vol. III, Part II, Solar house heating. Solar water heating. Solar stoves. Solar distillation. 169 pp. vol. IV, Photochemical processes. 187 pp. vol. V, Electrical processes. 170 pp. Sponsored by Univ. of Arizona, Stanford Research Inst., and Assoc. for Applied Solar Energy, 31 October-1 November 1955, Tucson, Ariz. Edwin F. Carpenter, Ed. Univ. of Arizona Press, Tucson, 1958. \$12.50 per set.

What We Do Know about Heart Attacks. John W. Gofman. Putnam's, New York, 1958. 191 pp. \$3.50.

Miscellaneous Publications

(Inquiries concerning these publications should be addressed, not to Science, but to the publisher or agency sponsoring the publication.)

Vibration and Shock Isolation—A Survey. National Standards Laboratory Tech. Paper No. 10. J. A. Macinate. 39 pp. *Tasmanian Farm Dams in Relation to Fish Culture.* Division of Fisheries and Oceanography Tech. Paper No. 4. 24 pp. Commonwealth Scientific and Industrial Research Organization, Melbourne, Australia, 1958.

Microscopic Staining Techniques. No. 3. Edward Gurr. Edward Gurr, Ltd., Michrome Laboratories, London, S.W. 14, ed. 2, 1958. 62 pp.

Explorer IV—1958 Epsilon Orbital Data Series. Issue 3, 16 September 1958. Army Ballistic Missile Agency, Redstone Arsenal, Ala.; Smithsonian Astrophysical Observatory, Cambridge, Mass., 1958. 871 pp.

Kenya Wild Life Society, Report, 1957. Consular House, Coronation Avenue, P.O. Box 20110, Nairobi, Kenya, 1958. 106 pp.

Roscoe B. Jackson Memorial Laboratory, Bar Harbor, Maine, Twenty-ninth Annual Report. The Laboratory, Bar Harbor, Maine, 1958. 92 pp.

Immunization Information for International Travel. Publ. No. 384. Prepared by the Epidemiology and Immunization Branch, Division of Foreign Quarantine. Bureau of Medical Services, U.S. Public Health Service, Washington, rev. ed., 1958 (order from Supt. of Documents, GPO, Washington 25). 71 pp. \$0.30.

Field Trip Guidebook, St. Louis Meeting, 1958. Field Trip Committee, Geological Soc. of America, New York 27, 1958. 46 pp.

Homemaking Education Programs for Adults. Vocational Division Bull. No. 268. Home Economics Education Series No. 30. Office of Education, Washington, 1958 (order from Supt. of Documents, GPO, Washington 25). 62 pp. \$0.25.

Concept of the Pacific. Bernice P. Bishop Museum annual report for 1957. Bishop Museum Press, Honolulu, Hawaii, 1958. 31 pp.

Mémorial de la Météorologie Nationale. Contribution à l'étude du climat d'entre Loire inférieure et Gironde d'après des archives climatologiques inédites. No. 44. Paule Garenc. Météorologie Nationale, Paris, 1957. 197 pp.

Laboratory Instructions in Microbiology. Louis P. Gebhardt and Dean A. Anderson. Mosby, St. Louis, Mo., ed. 2, 1958. 261 pp. \$3.75.

Practice in Thinking. A laboratory course in introductory chemistry. Jay A. Young. Prentice-Hall, Englewood Cliffs, N.J., 1958. 92 pp. \$2.95.

Albertus van Beek, 1787-1856. Mededelingen der Koninklijke Nederlandse Akademie van Wetenschappen, vol. 21, No. 5. J. G. Van Cittert-Eymers. Noord-Hollandsche, Amsterdam, 1958. 36 pp. Fl. 3.

Investigations of Ring-Necked Pheasants. Tech. Bull. No. 1, July 1958. William B. Robertson, Jr. Division of Game Management, Springfield, Ill., 1958. 138 pp. Single copies free from Director, Department of Conservation.

Reports

Sexual Agglutination of Heterothallic Yeasts in Diverse Taxonomic Areas

Abstract. Species in four genera of yeasts produce mating types that clump when brought together in liquid or on solid media. All species of a phylogenetic line of *Saccharomyces* are sexually agglutinative. Unisexuals of the latter species are believed to have from one to four sets of chromosomes, whereas bisexuals are believed to have from two to eight sets.

In 1956 I reported that cells of opposite mating types of *Hansenula wingei* Wickerham agglutinate immediately when mixed (1). This clumping reaction led to the fastest production of zygotes and diploid vegetative cells that I had yet observed in any yeast. Ascospore isolates of other strains of *H. wingei* from the same geographic area yielded mating types which were not agglutinative and which were exceedingly weak in their mating reaction. Opposite sexes, consisting of agglutinative and nonagglutinative haploid cultures, were crossed to yield a diploid hybrid, and ascospore isolates were obtained from this hybrid by a heat-treatment procedure (2) which kills vegetative cells but does not kill all the spores. When these ascospore cultures were studied, 96 percent were agglutinative; of these, 70 percent agglutinated immediately when they were mixed with a tester of the opposite sex and 26 percent agglutinated within a few minutes. Apparently in nature the agglutinative form gradually eliminates the nonagglutinative form by mating with it. Since the nonagglutinative haploids react sexually so very little,

their existence is hardly endangered by the agglutinative type.

As far as can be surmised from knowledge of phylogenetic lines, the four species in which agglutinative strains have now been found are recently evolved. The weakest sexual agglutination is shown by a new haploid species (NRRL Y-2408) which is yet to be described. The cells become agglutinative many hours after the opposite sexes are mixed—just before or when asci are formed.

Citeromyces matritensis Santa Maria (3) yields ascospores that are sexually agglutinative. The reaction of agar-grown haploid cells is immediate but not as dramatic as it is with *Hansenula wingei*, where the cells immediately adsorb or bind water and the mixture of opposite mating type cells becomes dry and viscous. The mixture of *Citeromyces matritensis* does not bind water appreciably and consequently retains the creamy consistency of each individual mating type. When the mixed cells are put in water, however, they are seen to be agglutinated. Reciprocally, liquid cultures of *C. matritensis* agglutinate in a much more striking manner than do those of *Hansenula wingei*. When shaken cultures are mixed, the cells agglutinate instantly and settle to the bottom. This impressive reaction is probably due in part to the fact that *Citeromyces matritensis* cells tend to grow in large colonies in liquid media.

The haploid form of *C. matritensis* is known by the name of *Torulopsis globosa* (Olsen et Hammer) Lodder et Kreger-van Rij (4). The single strain in our collection agglutinates and sporulates with one of the mating types derived from Santa Maria's diploid.

Not one of the three species already discussed equals in interest *Saccharomyces kluyveri* Phaff, Miller, and Shifrine (5). This species is sufficiently plastic genetically to yield many interesting forms, yet rigid enough so that all forms mentioned in this report may be kept pure. In common with the other more recently evolved species of its genus, *S. kluyveri* produces unisexual diploids. Unisexuals which are believed to be triploid and tetraploid are also produced. Each ploidy level is morphologically distinct, and all are sexually agglutinative. The unisexual diploids agglutinate and

mate abundantly with haploids or with unisexual diploids of the opposite sex. Four to six hours after opposite sexes are mixed the cells are streaked on agar. Two days later the largest colonies, which consist of triploid and tetraploid cells, depending on the ploidy of the cells that were mixed, are selected. Bisexuals are not agglutinative and hence are readily differentiated from their agglutinative parents. Each ploidy level by itself produces four-spored asci, whether unisexual or bisexual. The haploids produce conjugated asci. Higher unisexual ploidy levels originate through conjugation of cells of various degrees of ploidy. The zygotes may produce buds rather than ascospores and thus may give rise to vegetative forms. When unisexuals having more than one set of chromosomes sporulate, the asci are not conjugated, but consist of a single cell.

Saccharomyces kluyveri grows rapidly and is a rather strong fermenter. These characteristics, plus the agglutinative reaction, give the species industrial possibilities. For example, growth rates of its unisexual diploids compare favorably with those of *Candida (Torulopsis) utilis*, the common food yeast. The two sexes of *Saccharomyces kluyveri* may be grown separately and then combined in a tank. Following agglutination and settling, the supernatant could be run off; hence, the amount of centrifugation required for harvesting the crop would be greatly reduced. Naturally, such utilization depends upon the cells' being of desirable nutritional composition. The composition has not been determined. *Saccharomyces kluyveri* exhibits exceedingly strong sexual reactions, has the ability to produce polyploids more abundantly than any other yeast known, and holds a potential for commercial uses. Because of these factors, *S. kluyveri* and closely related species possessing the property of sexual agglutination may prove superior to all other known species for genetic, and possibly also for industrial, studies.

The heat-treatment procedure devised for the isolation of mating types from diploid species of *Hansenula* (2) is equally effective for *Saccharomyces*, and no modification is required. The more strongly heterothallic strains of *S. cerevisiae*, *S. carlsbergensis*, and *S. diastaticus*, which geneticists generally use, readily yield colonies of opposite mating types on heat treatment of sporulated cultures at 60° or 63°C. Plates are streaked at 0, 1, 2, 3, 4, 5, 6, 8, 10, 12, 15 minutes, and thereafter at 5-minute intervals through 60 minutes. Fifteen minutes at 57°C is adequate for *S. kluyveri*. Most of the colonies on the terminal plates consist of one or the other mating type.

At present four species of yeasts, occurring in four genera, have been found to

Instructions for preparing reports. Begin the report with an abstract of from 45 to 55 words. The abstract should not repeat phrases employed in the title. It should work with the title to give the reader a summary of the results presented in the report proper. (Since this requirement has only recently gone into effect, not all reports that are now being published as yet observe it.)

Type manuscripts double-spaced and submit one ribbon copy and one carbon copy.

Limit the report proper to the equivalent of 1200 words. This space includes that occupied by illustrative material as well as by the references and notes.

Limit illustrative material to one 2-column figure (that is, a figure whose width equals two columns of text) or to one 2-column table or to two 1-column illustrations, which may consist of two figures or two tables or one of each.

For further details see "Suggestions to Contributors" [*Science* 125, 16 (1957)].

possess the sexual agglutination reaction. This mating mechanism is fairly common among yeasts, especially among species evolved in terms of recent geological time.

LYNFERD J. WICKERHAM
Fermentation Laboratory, Northern
Utilization Research and Development
Division, U.S. Agricultural Research
Service, Peoria, Illinois

References and Notes

1. L. J. Wickerham, *Compt. rend. trav. lab. Carlsberg, Sér. physiol.* 26, 423 (1956).
2. L. J. Wickerham and K. A. Burton, *J. Bacteriol.* 67, 303 (1954).
3. J. Santa Maria, *Inst. nacl. invest. agron. (Madrid) Sec. bioquím.* 17, 269 (1957).
4. J. Lodder and N. J. W. Kreger-van Rij, *The Yeasts, A Taxonomic Study* (Interscience, New York, 1952), p. 426.
5. H. J. Phaff, M. W. Miller, M. Shifrine, *Antonie van Leeuwenhoek J. Microbiol. Serol.* 22, 145 (1956).
6. The assistance of Mr. K. A. Burton and Mrs. Jane Roberson is gratefully acknowledged.

23 June 1958

Hormonal Control of Onset of Corneal Reflex in the Frog

In a previous study (1) it was reported that the corneal (wink) reflex is unelicitable in the tadpole until just before the period of metamorphic climax. In *Rana pipiens* the onset of the reflex normally precedes forelimb emergence from the branchial chamber by an average of 4 days (range, 0 to 10 days). In *R. catesbeiana* this is also true, except for rare instances of earlier onset. It was further established (1, 2) that the onset of the reflex was strictly related to metamorphosis; it never appeared in the non-metamorphosing hypophysectomized tadpole, and the time of onset could be moved forward by treatment of the whole normal tadpole with thyroxine, but the extent of acceleration was less than for other metamorphic changes.

However, local stimulation of the reflex center in the medulla oblongata of large midlarval tadpoles with pellets containing thyroxine produced a premature maturation of the center, as well as an unusually early onset of the reflex; maturation occurred as much as 18 days before forelimb emergence. These results demonstrated the dependence of the reflex center upon thyroid hormone for its final maturation.

It has been shown that the later stages of induced metamorphosis in thyroidless or hypophysectomized tadpoles are passed through progressively more slowly than the early stages, at a constant thyroxine dosage level (3), and that successive events or stages of metamorphosis tend to have a higher thyroxine concentration requirement or threshold (4). Hence it may be assumed that the later metamorphic event, forelimb emergence, displays a higher threshold than does the onset of the corneal reflex, the earlier metamorphic event.

To test this assumption, concentrations of thyroxine were sought which would in fact permit the establishment of the corneal reflex without concomitantly stimulating the rupture of the skin windows through which the forelimbs emerge. In tests of over 150 *R. pipiens* and a few *R. catesbeiana*, over a large range of thyroxine concentrations in the surrounding water (from 0.002 to 2 µg/lit., water and food being changed daily, with thyroxine added immediately thereafter), the validity of the assumption has been demonstrated in two instances (see data in Table 1 for 108- and 177-day animals). In six other instances a related and very significant lengthening of the interval between the onset of the reflex and forelimb emergence has been recorded. In general, it has been found that, at 25°C, concentrations of dl-thyroxine of 0.6 µg/lit. invariably bring about forelimb emergence, if permitted

to act for a long enough time. Concentrations of 0.4 µg/lit. rarely produce forelimb emergence, although incipient thinning of the skin-window area is usually obtained. A concentration of 0.2 µg/lit. is insufficient to initiate the corneal reflex or forelimb emergence. At 15°C, even 1.0 µg/lit. is ineffective in producing rupture of the skin window.

The study discussed in this report provides further evidence in support of the belief that most metamorphic changes in the frog tadpole are separable events, capable of being brought about individually by local hormone treatment (2, 5), or capable of being separated from succeeding metamorphic events by careful manipulation of hormone concentration and temperature (6).

JERRY J. KOLLROS

Department of Zoology,
State University of Iowa,
Iowa City

References and Notes

1. J. Kollros, *J. Exptl. Zool.* 89, 37 (1942).
2. —, *Physiol. Zool.* 16, 269 (1943).
3. W. Etkin, *J. Exptl. Zool.* 71, 317 (1955).
4. J. Kollros, *Anat. Record* 125, 624 (1956).
5. H. Hartwig, *Biol. Zentr.* 60, 473 (1940); M. Lüke, *Wilhelm Roux' Arch. Entwicklungsmech. Organ.* 142, 730 (1944); J. Kollros and J. C. Kaltenbach, *Physiol. Zool.* 25, 163 (1952); J. C. Kaltenbach, *J. Exptl. Zool.* 122, 21, 41, 449 (1953); J. Kollros and V. M. McMurray, *ibid.* 131, 1 (1956); I. Pesetsky and J. Kollros, *Exptl. Cell Research* 11, 477 (1956).
6. The work reported here was supported in part by a grant from the National Science Foundation and by the Old Gold Development Fund, State University of Iowa.

3 July 1958

Factors Affecting the Relative Deposition of Strontium and Calcium in the Rat

Abstract. Varying the calcium, phosphorus, carbonate, and lactate content of the diet was shown to affect the deposition in bone of Sr^{90} to a degree quite different from concurrent effects on Ca^{45} deposition. The influence of these findings on the evaluation of the Sr^{90} fallout hazard is discussed.

In a recent report in *Science* we presented evidence against the commonly accepted concept that the deposition and retention of Sr^{90} in bone is simply related to the concomitant deposition and retention of calcium (1). This concept has been widely employed in the evaluation of the hazard to human beings of Sr^{90} from fallout. We now wish to report further experiments, of an admittedly preliminary nature, which support our earlier position and which suggest an explanation for the varied results which have been reported by investigators in this field (see 2).

Six groups of four rats each were maintained for 8 days on diets which varied in one or more of the following constituents: calcium, phosphorus, car-

Table 1. Record of treatment of hypophysectomized tadpoles, demonstrating separability of the onset of the corneal reflex from the emergence of the forelimbs. Thyroxine was added to the water in which the animals were raised.

Species (<i>Rana</i>)	Form of thyroxine	Thyroxine concn. (µg/lit.)	Tempera- ture (°C)	Treatment time in days	
				Before reflex onset	Between reflex onset and forelimb emergence
<i>R. pipiens</i>	dl	1.0	25	73	41
<i>R. pipiens</i>	dl	1.0	15	161	37*
<i>R. pipiens</i>	dl	1.0	25	71	45
<i>R. pipiens</i>	dl	1.0	25	47	44*
<i>R. pipiens</i>	l	0.2	25	71	47
<i>R. pipiens</i>	l	0.4	15	170	108*
<i>R. pipiens</i>	l	0.4	25	87	43
<i>R. catesbeiana</i>	dl	0.4	15	70	177†

* Tadpole died prior to emergence of forelimbs.

† The metamorphic progress came to a complete standstill at 15°C; skin windows thinned only slightly. The tadpole was transferred to a 25°C bath after 164 days; forelimb emergence occurred 13 days later.

Table 1. Summary of experiment and results.

Group No.	Composition of diet (%)					Ingested isotopes per gram of bone ash (%)		
	Ca	P	Ca/P	Carbonate	Lactate	Sr ⁹⁰	Ca ⁴⁵	Sr ⁹⁰ /Ca ⁴⁵
1	0.1	0.12	0.8		0.38	1.8 ± 0.2	8.1 ± 1.0	0.22 ± 0.02
2	0.1	0.12	0.8	0.13		2.3 ± 0.3	9.1 ± 1.0	0.25 ± 0.02
3	0.1	0.12	0.8	3.1		1.5 ± 0.3	4.4 ± 0.9	0.34 ± 0.02
4	2.0	0.12	17		8.8	1.0 ± 0.1	1.7 ± 0.2	0.60 ± 0.02
5	2.0	0.12	17	3.0		0.74 ± 0.16	1.6 ± 0.2	0.46 ± 0.07
6	2.0	2.4	0.8	3.0		0.34 ± 0.04	0.84 ± 0.19	0.41 ± 0.04
A†	0.1	0.5	0.2		0.38	0.87 ± 0.19‡	4.4 ± 0.7	0.20 ± 0.02‡
B†	2.0	0.5	4.0		8.8	0.43 ± 0.15‡	0.79 ± 0.28	0.55 ± 0.09‡

* All values are for an average of four animals, plus or minus one standard deviation.

† Results of previously reported experiment (see 1).

‡ Strontium-90 rather than Sr⁹⁰ was employed in these experiments (see 1).

bonate, and lactate. The composition of the diets with respect to these variables is indicated in Table 1. For the 3 days prior to sacrifice, Sr⁹⁰ and Ca⁴⁵ were added to all of the diets. Other details of diet and procedure were as previously described (1). The rats employed were mature females of the Sprague-Dawley strain.

The concentrations of Sr⁹⁰ and Ca⁴⁵ in the femur, at sacrifice, expressed as percentages of total isotope fed, are recorded in Table 1. Also shown, as groups A and B, are comparable data from the previously reported experiment (1). Animals in groups A and B were sacrificed after 3 days on a Sr⁹⁰, Ca⁴⁵ regimen; however, their period on the experimental diet prior to the addition of radioisotopes was 30 days, rather than the 5-day conditioning period employed for groups 1 through 6.

The previously reported effect of dietary calcium level on the ratio of Sr⁹⁰/Ca⁴⁵ deposition in bone (see data for groups A and B) is confirmed by the results from groups 1 and 4. The animals fed a 2.0-percent calcium level diet show a Sr⁹⁰/Ca⁴⁵ ratio nearly three times that of the animals fed the 0.1-percent calcium level diet. The lower phosphate content of the diets of groups 1 and 4 as compared with the diets of groups A and B had no apparent effect on the Sr⁹⁰/Ca⁴⁵ ratio but did increase by a factor of two the absolute deposition of both Sr⁹⁰ and Ca⁴⁵.

In groups A, B, 1, and 4, supplementary calcium was added as the lactate. Groups 2 and 5 correspond, respectively, to groups 1 and 4, except that supplementary calcium was added as the carbonate. The effect of dietary calcium level on the Sr⁹⁰/Ca⁴⁵ ratio in bone is again evident in groups 2 and 5, although the difference in the ratios is somewhat less with calcium carbonate supplementation than with calcium lactate supplementation. The effect of carbonate (added as Na₂CO₃), independent of

changes in calcium level, is seen in the comparison of group 3 with group 2. Added carbonate reduces deposition of both Sr⁹⁰ and Ca⁴⁵, but the effect on Ca⁴⁵ deposition is significantly greater than the effect on Sr⁹⁰ deposition.

The effect of phosphate (added as Na₂HPO₄), independent of changes in level of calcium or carbonate, is seen in the comparison of groups 5 and 6. A 20-fold increase in phosphate reduced both Sr⁹⁰ and Ca⁴⁵ deposition by a factor of about two, leaving the ratio of Sr⁹⁰ to Ca⁴⁵ in bone essentially unchanged. At a constant phosphate level and a constant high carbonate level, the effect of variation in calcium level on the Sr⁹⁰/Ca⁴⁵ ratio in bone is greatly reduced (compare groups 3 and 5), and with a constant Ca/P ratio, and high carbonate, the increase in the Sr⁹⁰/Ca⁴⁵ ratio, with increased calcium level, is even smaller (compare groups 3 and 6).

Experiments reported by Wasserman *et al.* (2) were performed at a constant Ca/P ratio; this may explain in part the absence in their experiments of effects of dietary calcium level on the ratio of Sr to Ca deposited. It should also be noted that the rats in our experiments were mature, nongrowing animals, while those employed in the experiments of Wasserman *et al.* were rapidly growing animals which deposited much larger fractions of the administered radioisotopes.

Our present results, while they can hardly be said to clarify the situation, do serve to emphasize the complexity of the interrelationships involved. If, for purposes of hazard evaluation, this complexity makes expedient the temporary adoption of simplifying assumptions, such as the assumption that calcium will behave biologically as an isotopic diluent of Sr⁹⁰, the uncertainties introduced with such assumptions must be kept clearly in mind. Thus, in groups 2, 3, 5, and 6 of the present experiment, changes in the calcium, sodium, phosphate, and/or car-

bonate concentrations in the diet resulted in a nearly three-fold variation in the percentage ratio of Sr⁹⁰/Ca⁴⁵ deposition in bone, and a nearly sevenfold variation in the absolute quantity of Sr⁹⁰ deposited. Although the elevation of calcium levels in the diet did decrease Sr⁹⁰ deposition, the effect of a 20-fold increase in calcium was only a twofold decrease in Sr⁹⁰ deposition, and effects of similar magnitude were obtained by varying the phosphate and carbonate levels in the diet. While these are results of short-duration experiments, previous experiments involving feeding of Sr⁹⁰ and Ca⁴⁵ for periods of up to 24 days gave similar results with a more limited set of variables (1). For a reasonably adequate evaluation of this problem, additional variables must be studied over time periods embracing the life span of the experimental animals employed. Such experiments are being conducted in this laboratory (3).

RAY F. PALMER

ROY C. THOMPSON

HARRY A. KORNBERG

Hanford Laboratories,
General Electric Company,
Richland, Washington

References and Notes

1. R. F. Palmer, R. C. Thompson, H. A. Kornberg, *Science* 127, 1505 (1958).
2. R. H. Wasserman, C. L. Comar, D. Papadopoulos, *ibid.* 126, 1180 (1957).
3. This report is based on work performed under contract No. W-31-109-Eng-52 for the U.S. Atomic Energy Commission. The technical assistance of Joan Hess is gratefully acknowledged.

7 July 1958

Phenylalanine Hydroxylation Cofactor in Phenylketonuria

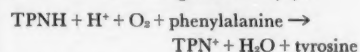
Abstract. The enzymatic conversion of phenylalanine to tyrosine had previously been shown to require a nonprotein cofactor. It has now been demonstrated by direct assay that the cofactor is present in phenylketonuric liver samples. The lack of a functional phenylalanine hydroxylating system in phenylketonuria is not due to the absence of the cofactor.

Recent enzymological studies have strongly supported the suggestion, originally made by Jervis in 1947 (1), that in the disease phenylketonuria there is a block in the conversion of phenylalanine to tyrosine.

In 1953, results were reported of both *in vitro* (2) and *in vivo* (3) studies which showed that this reaction is completely missing or markedly decreased in phenylketonuria. After the system which catalyzes the hydroxylation of phenylalanine to form tyrosine was shown to require at least two protein fractions (4, 5), it was demonstrated by direct assay that only one of these enzymes was

missing in liver samples from phenylketonuric patients (6, 7).

Studies (5) on the stoichiometry of the enzymatic conversion of phenylalanine to tyrosine have led to the formulation of the following reaction (8):



In 1958, it was reported that in addition to the two enzyme fractions already referred to, this enzyme system requires a new nonprotein cofactor which has been purified extensively from rat liver (9). More recently, it has been shown that tetrahydrofolic acid (10) and some other tetrahydropteridines (11) can replace the rat-liver cofactor in this reaction. Although none of the reduced pteridines which have been tested, including tetrahydrofolic acid, appears to be structurally identical with the natural cofactor, or as active in the enzyme system, their availability in relatively large amounts has made it possible to carry out experiments which have led to an understanding of the general role of the two enzymes in the over-all reaction. Evidence has been obtained from experiments in which stoichiometric amounts of tetrahydropteridines were employed which suggests that neither the sheep enzyme nor TPNH is directly involved in the hydroxylation reaction. The sheep enzyme catalyzes a reaction which serves to keep the coenzyme in an active form. In the presence of large amounts of the tetrahydropteridines, the rat enzyme alone can catalyze the conversion of phenylalanine to tyrosine (11).

The discovery that a cofactor is intimately involved in the enzymatic formation of tyrosine raised the possibility that the absence of a functional phenylalanine hydroxylating system in phenylketonuria might be due to the absence of this cofactor rather than to the absence of one of the enzymes. The present report deals with the question of

Table 2. Activity of phenylalanine hydroxylase in liver homogenates from phenylketonuric and nonphenylketonuric children. Homogenate (0.3 ml) was added to reaction mixtures which contained the following components (in micromoles): phosphate buffer (pH 6.8), 100; L-phenylalanine, 2.0; glucose, 75; TPN, 0.3; DPN, 0.3; nicotinamide, 5.0; glucose dehydrogenase in excess. Purified rat or sheep enzymes and cofactor were added where indicated. The final volume was 1.0 ml, and the tubes were shaken in air at 25°C for 1 hour. All values are expressed as micromoles of tyrosine formed. Although this is not shown in the table, the purified rat enzyme with or without added cofactor is essentially inactive. The same is true of the sheep enzyme. The whole experiment on each liver sample was completed in 1 day. In each case the figure on the bottom line represents the activity of the purified rat and sheep enzymes which were used in that particular experiment.

Additions	Enzyme activity ($\Delta \mu\text{m}$ of tyrosine/60 min)			
	Phenylketonuric subjects		Nonphenylketonuric subjects	
	M. C. (3 yr)	R. R. (5 yr)	B. S. (8 yr)	S. M. (15 yr)
Liver homogenate	0.020	0.018	0.069	0.059
Liver homogenate + cofactor	0.022	0.026	0.165	0.177
Liver homogenate + rat enzyme	0.310	0.078		
Liver homogenate + rat enzyme and cofactor	0.618	0.480	0.661	0.560
Liver homogenate + sheep enzyme	0.020	0.020	0.070	0.068
Liver homogenate + sheep enzyme + cofactor	0.021	0.018	0.169	0.157
Rat enzyme + sheep enzyme + cofactor	0.700	0.550	0.448	0.355

whether the cofactor or the enzyme is missing in the disease.

Human liver biopsy samples of approximately 1 g were obtained during laparotomy (12) and immediately frozen. The tissue could be kept frozen without apparent loss of cofactor activity for several weeks before being used. For the cofactor assay, the liver sample was partially thawed and homogenized with 2 volumes of cold glass-distilled water in a glass homogenizer. The mixture was then placed in a boiling-water bath for 1½ minutes, cooled, and centrifuged. A suitable aliquot of the yellow, opalescent supernatant fluid was then assayed for cofactor activity (9). For the determination of enzyme activities, a separate liver sample was homogenized with three volumes of cold 0.9-percent KCl, and a sample of the homogenate was then assayed by a procedure similar to that which has previously been used for sheep- and rat-liver extracts (5), the only modification being the addition of nicotinamide and of both DPN and TPN. Because of the relatively low activity, the time of incubation was increased to 60 minutes.

The results of the cofactor determinations are shown in Table 1. For purposes of comparison, the activity of a boiled extract of rat liver is also included. It is clear that the cofactor is not missing in the phenylketonuric liver samples. Indeed, from this limited series it seems as though there may be more cofactor present in phenylketonuric liver than in the control samples.

The results of studies on the enzyme

activity of the human liver homogenates are shown in Table 2. The phenylketonuric liver homogenates appear to have some ability to catalyze the conversion of phenylalanine to tyrosine. Although this would be consistent with the *in vitro* studies, which indicated that the enzymatic block is not a complete one in the disease (3), it should be pointed out that this low level of activity approaches the sensitivity limits of the methods which were used. This slight activity is not significantly increased by the addition of the cofactor or the sheep enzyme, or both (13). The addition of the purified rat enzyme, even without any additional cofactor, leads to a large increase in activity, which also indicates that the phenylketonuric liver contains the cofactor (14).

These results are in agreement with those of previous studies (6) which have led to the conclusion that it is the rat enzyme which is almost completely non-functional in phenylketonuria; the sheep enzyme and the cofactor are present. In the light of our present understanding of the role of these two enzymes in the conversion of phenylalanine to tyrosine, it may be emphasized that the enzyme which is not active in phenylketonuria is that one which is intimately involved in the hydroxylation reaction. The relationship between this enzymatic defect and the pathophysiology of the disease, however, remains obscure.

SEYMOUR KAUFMAN

Laboratory of Cellular Pharmacology,
National Institute of Mental Health,
Bethesda, Maryland

Table 1. The cofactor activity of phenylketonuric and "normal" human liver.

Subject	Age of subject (yr)	Cofactor activity [units*/mg (dry weight)]
<i>Human phenylketonuric biopsy liver</i>		
J. P.	3	0.027
P. H.	5	0.033
<i>Human nonphenylketonuric biopsy liver</i>		
B. S.	8	0.015
S. M.	15	0.007
<i>Rat liver</i>		0.018-0.022

* A unit of cofactor activity has been defined as the amount which leads to the formation of an additional micromole of tyrosine over a blank without any added cofactor under the conditions of the standard assay.

References and Notes

1. G. A. Jervis, *J. Biol. Chem.* 169, 651 (1947).
2. —, *Proc. Soc. Exptl. Biol. Med.* 82, 514 (1953).
3. S. Udenfriend and S. P. Bessman, *J. Biol. Chem.* 203, 961 (1953).
4. C. Mitoma, *Arch. Biochem. Biophys.* 60, 476 (1956); S. Kaufman, *Biochim. et Biophys. Acta* 23, 445 (1957).
5. —, *J. Biol. Chem.* 226, 511 (1957).
6. H. W. Wallace, K. Moldave, A. Meister, *Proc. Soc. Exptl. Biol. Med.* 94, 632 (1957); C. Mitoma, R. M. Auld, S. Udenfriend, *ibid.* 94, 634 (1957).
7. Although the two enzyme systems which have been described [by C. Mitoma, *Arch. Biochem. Biophys.* 60, 476 (1956), and S. Kaufman, *J. Biol. Chem.* 226, 511 (1957)] which are capable of catalyzing the conversion of phenylalanine to tyrosine are similar, they do differ in several respects. The first appears to be specific for DPNH, while in the second, TPNH is more active. More pertinent to the present discussion are differences in nomenclature. The two enzymes in the system described by Kaufman were purified from different sources, one from rat liver and the other from sheep-liver, extracts. Throughout the text of this report these are referred to as the rat and sheep enzymes, respectively. In all probability, the purified rat enzyme of Kaufman is equivalent to Mitoma's rat fraction I (the labile enzyme), while the enzyme purified from sheep-liver extracts by Kaufman is equivalent to Mitoma's rat fraction II (the stable enzyme).
8. The following abbreviations are used in this report: DPN and DPNH, oxidized and reduced diphosphopyridine nucleotide, respectively; TPN and TPNH, oxidized and reduced triphosphopyridine nucleotide, respectively.
9. S. Kaufman, *J. Biol. Chem.* 230, 931 (1958).
10. —, *Biochim. et Biophys. Acta* 27, 428 (1958).
11. —, in preparation.
12. I would like to thank Dr. C. Everett Koop of the Children's Hospital of Philadelphia for the liver biopsy samples which made this study possible.
13. Although this is not shown in Table 1, in a few experiments the addition of THF did not restore the activity when added to the phenylketonuric liver homogenates.
14. It may be noted that the group of phenylketonurics used in this study is younger than the group of normals. Supplementary, unpublished data indicate that the age of the subjects (within the limits described in Tables 1 and 2) has no effect on the results which have been obtained.

28 July 1958

A Consideration of the Metabolic Rates of Some Shrew Tissues

Abstract. Metabolic rates of certain tissues of a shrew, *Cryptotis*, were lower than had been expected in view of the high total metabolism characteristic of shrews. Similar trends were shown in the rodent *Reithrodontomys*. The depression of metabolism of some tissues that was observed in these very small mammals may aid them in conserving energy during periods of inactivity.

The general inverse correlation between metabolic rate of an intact animal and body weight has been well demonstrated (1). Among the mammals whose respiratory rates have been measured, shrews of the family Soricidae appear to occupy a unique position (2). The asymptotic nature of the

body-weight-metabolic-rate curve calculated for shrews suggests that the smallest species measured lie close to the theoretical lowest limit of adult mammalian size. Even the larger species exhibit a metabolic rate well above that of rodents of equal weight (2). In view of these findings, the relationship between the total metabolic rates and those of isolated tissues in shrews is of interest.

This report is concerned with presentation of some preliminary data on O_2 consumption of isolated liver, diaphragm, kidney, and lung tissues of the shrew *Cryptotis parva*, together with comparative information on similar tissues from the harvest mouse (*Reithrodontomys humilis*), white mouse (*Scalopus aquaticus*), white rat, and domestic rabbit. Determinations were made on the tissues of seven shrews of both sexes, weighing from 4.1 to 5.0 g. The specimens were wild-caught and were maintained from 1 to 6 wk in the laboratory before sacrifice. The animals were killed by crushing the cervical vertebrae; the organs were immediately removed and placed in cold Ringer's phosphate-glucose (0.1M) solution (3). The tissues were prepared by the hand-slicing technique (3). Respiratory rates were measured by the direct Warburg method at a temperature of $37 \pm 0.03^\circ C$, air being utilized as the gas phase. Three milliliters of Ringer's phosphate-glucose solution constituted the vessel medium. Flasks were shaken at 120 cy/min, and 15 minutes of equilibration time were allowed, after which readings were taken at 15-minute intervals for 1 hour.

The results are presented in Fig. 1. Although differing absolutely to a considerable extent, the relative metabolic rates of the various tissues of white mouse, white rat, and rabbit appear to present the same qualitative relationship to body weight as does metabolism of the intact animal. A similar trend was obtained by Kleiber (4) for liver slices over a size range of larger species, although his values for rat and rabbit liver tissue were higher than those obtained in the present study. With the exception of the value for kidney, the values for shrew tissues fall below the extrapolated curve of the three species mentioned above. This effect is most marked in the case of liver. In view of the small size and high metabolic rate of the intact shrew, this departure is rather striking and would seem to indicate that the high respiratory rates exhibited by shrews must be due to "extrinsic" factors such as nervous stimulation, hormone levels, or concentrations of metabolites in blood or tissue fluids rather than to generally higher "inherent" rates of tissue metabolism. Because of the significantly greater metabolic rates for shrews as compared with those

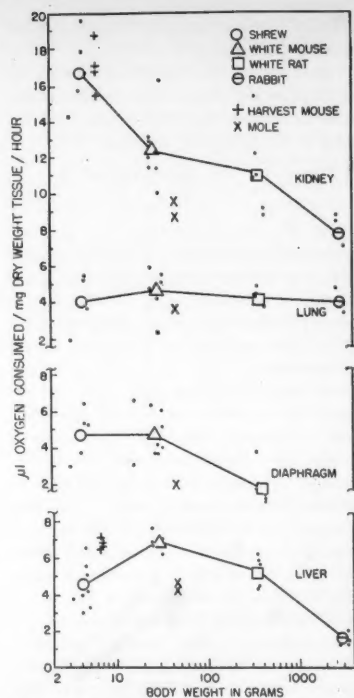


Fig. 1. Tissue metabolic rates of several small mammals.

for other mammals of similar size, the preceding statement would be valid even if the observed rates for shrew tissues fell in the position on the curve that would be predicted on the basis of size alone. The fact that they actually lie below this curve is even more unexpected.

These observations suggest two alternative explanations. Both are highly speculative in view of the limited data available for shrew and other mammalian tissues and for total respiratory rates measured under comparable conditions. On the one hand, the observed rates for lung, diaphragm, and liver tissues of the shrew may be a reflection of the relatively primitive status of the insectivores among mammals, the high metabolic rate exhibited by the intact shrew representing an adaptation of controlling mechanisms to elevate metabolic processes in order to compensate for heat loss or other factors in the physiology of these small creatures. Alternatively, the relatively low respiratory rates exhibited by three of the four tissues measured may in themselves be an adaptation from a "primitive" condition in which higher rates existed. In any case, the functional significance of this situation would seem to lie in a possible marked lowering of metabolism when the animals are inactive, thus resulting in a considerable

conservation of energy by the individual.

Observations indicate that shrews of the genera *Cryptotis* and *Blarina* often sleep very soundly and may awaken slowly, making feeble or trembling, uncoordinated movements before becoming fully active (5). This behavior is reminiscent of that of a bat emerging from a torpid state and may similarly indicate a reduction in metabolic rate in the inactive condition. We have made measurements which indicate that the shrew, unlike the bat, shows no marked reduction in body temperature during sleep. Determinations of respiratory rates of sleeping or lightly anesthetized shrews would be highly instructive in this connection.

The data for liver and kidney tissues of *Reithrodontomys*, a mammal which lies in the same weight range as *Cryptotis*, indicate trends similar to those for the latter. The metabolic rates for kidney are quite comparable, while the rates for liver show a similar, but less pronounced, departure from the expected. This suggests that the depression of certain tissue rates may, at least in part, be a general characteristic of small mammals and cuts across phylogenetic lines. Kleiber noted a tapering off and slight reversal of rates in liver slices of larger mammals (horse and cow). The present data suggest a similar phenomenon at the "small-sized" end of the curve. The values for diaphragm, kidney, and liver tissues from a single mole fall noticeably below the general curve. This may indicate that insectivores in general have inherently low metabolic rates for tissue, and this, in turn, may be a physiological indication of their primitive nature.

The correspondence of the high metabolic rates for kidney of shrew and harvest mouse with their expected position on the general curve is not understood. The explanation that the discrepancy is a result of diet, with consequent differences in the level of nitrogenous excretion, is made unlikely by the fact that the essentially carnivorous shrew and the herbivorous harvest mouse exhibit similar trends.

JAMES R. REDMOND

JAMES N. LAYNE

Department of Biology,
University of Florida, Gainesville

References

1. F. G. Benedict, *Carnegie Inst. Wash. Publ. No. 503* (1938); E. Zeuthen, *Compt. rend. trav. lab. Carlsberg, Sér. chim.* 26, 20 (1947).
2. O. F. Pearson, *Science* 108, 44 (1948).
3. W. W. Umbreit, R. H. Burris, J. F. Stauffer, *Manometric Techniques and Tissue Metabolism* (Burgess, Minneapolis, 1951).
4. M. Kleiber, *Proc. Soc. Exptl. Biol. Med.* 48, 419 (1941).
5. J. J. Christian, *J. Mammalogy* 31, 281 (1950); personal observations.

9 July 1958

Inhibition of Enzymatic Synthesis of Pantothenate by 2,3-Dichloroisobutyrate

Abstract. The investigations reported here have shown that 2,3-dichloroisobutyrate is uncompetitive with β -alanine and competitive with pantoate for a site on the enzyme of pantothenate synthesis. The enzyme dissociation constant of the inhibitor was comparable to that of the competitive substrate.

Evidence implicating pantothenate synthesis as a metabolic pathway involved in the herbicidal action of several chloro-substituted aliphatic acids was recently obtained from yeast growth experiments (1). One of these compounds, 2,3-dichloroisobutyrate, prevents pollen development without causing female sterility when applied to plants at low concentrations (2). This "gametocidal" property of the chemical has been evaluated for use in production of hybrid cotton seeds on male-sterile parent plants. A knowledge of biochemical mechanisms inhibited by dichloroisobutyrate could facilitate further development of the "gametocide" principle. The experiments reported here were initiated to determine the effect of 2,3-dichloroisobutyrate on the enzymatic synthesis of pantothenate.

The pantothenate-synthesizing enzyme was prepared from *Escherichia coli* (3), and its activity was determined manometrically at 30°C by following the rate of acid liberation of CO_2 from bicarbonate buffer (pH 8) in Warburg vessels containing a 5-percent CO_2 atmosphere. The reaction mixture was adjusted to a total volume of 3.0 ml containing 0.1M KCl, 0.01M MgSO_4 , 0.02M β -alanine, 0.02M pantoate, 0.01M adenosine triphosphate, 0.066M KHCO_3 , and sufficient enzyme to give the activity desired. The adenosine triphosphate was placed in a side arm during the equilibration period and tilted into the body of the flask to initiate the reaction.

Initial rates of CO_2 liberation were proportional to enzyme concentrations up to rates of 350 μl of CO_2 per hour. The enzyme concentration was adjusted to give rates of approximately 250 $\mu\text{l/hr}$, and readings were taken at 5-minute intervals for a 1-hour period. An additional 20 to 40 μl of CO_2 per hour was released by the adenosine triphosphatase, which contaminated each of the enzyme preparations. This CO_2 production was not inhibited by 2,3-dichloroisobutyrate. Appropriate corrections were made for adenosine triphosphatase activity in all tests.

Inhibition of the pantothenate-synthesizing enzyme by 2,3-dichloroisobutyrate (4) was tested under conditions in which one substrate (β -alanine or pantoate)

concentration was held constant at 0.02M and the other varied over a range of 0.00167 to 0.02M. The data presented in Fig. 1 were obtained from three independent determinations and combined for analysis by the method of Lineweaver and Burk (5). The family of parallel lines obtained when β -alanine was considered as substrate is generally known as "coupling inhibition" or "uncompetitive inhibition" and indicates that the inhibitor couples with the enzyme-substrate complex rather than with the free enzyme. Therefore, the inhibitor-enzyme complex must have occurred at a site independent of β -alanine. This site was evidently the point at which pantoate combines with the enzyme, since a typical competitive inhibition test was obtained when pantoate was considered as substrate for the reaction. This is apparently the first instance in which these two types of inhibition have been demonstrated in one enzymatic reaction by a single inhibitor.

The values obtained for the enzyme dissociation constant for this inhibitor (K_i), when three independent preparations of the enzyme were used, were 0.0014, 0.0019 and 0.0064M, respectively. The corresponding values for the dissociation constant for pantoate (K_m) were 0.0025, 0.0032 and 0.0060M, respectively. The variability of the latter values was in agreement with the values reported previously (3). A comparison of the K_i and K_m values obtained with the individual enzyme preparations

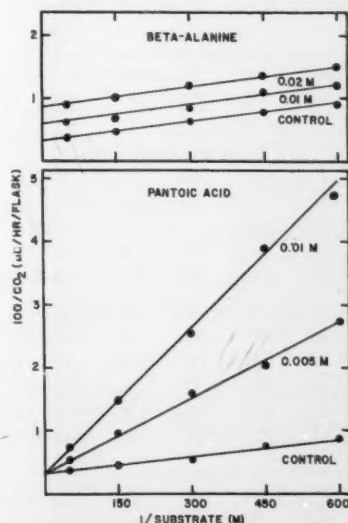


Fig. 1. Inhibition of the pantothenate-synthesizing enzyme at the indicated concentrations of 2,3-dichloroisobutyrate shows the inhibitor to be uncompetitive with β -alanine and competitive with pantoate.

shows that the inhibitor and the natural substrate have approximately the same affinity for the enzyme.

J. L. HILTON

*Crops Research Division,
Agricultural Research Service,
U.S. Department of Agriculture,
Beltsville, Maryland*

References and Notes

1. J. L. Hilton, L. L. Jansen, W. A. Gentner, *Plant Physiol.* 33, 43 (1958).
2. F. M. Eaton, *Science* 126, 1174 (1957); *Farm Chem.* 121, 15 (1958).
3. G. D. Novelli, in S. P. Colowick and N. O. Kaplan, Eds., *Methods in Enzymology* (Academic Press, New York, 1955), vol. 2, p. 619.
4. Chemically pure 2,3-dichloroisobutyric acid was obtained from Rohm and Haas Company, Philadelphia, Pa.
5. H. Lineweaver and D. Burk, *J. Am. Chem. Soc.* 56, 658 (1934).

28 July 1958

Variability of

Tooth Formation in Man

Data on the timing of tooth formation are of potential value in a wide variety of applications, ranging from the estimation of age in skeletal remains and accident victims (1) to the investigation of dental development in precocious puberty and endocrinopathies (2). However, it would appear that values for tooth formation commonly given in the

Table 1. Variability of mandibular tooth formation (in months) as found in the present study, and as commonly given.

Tooth	This study		Kron- feld (4) "Range":*
	No.	Percentile	
		5th 95th	
<i>Beginning calcification</i>			
\bar{P}_1	164	19 36	21- 24
\bar{P}_2	179	32 56	27- 30
\bar{M}_1	157	1 3	birth
\bar{M}_2	196	34 58	30- 36
\bar{M}_3	135	90 131	96-120
<i>Crown completion—root formation</i>			
\bar{P}_1	172	72 97	60- 72
\bar{P}_2	166	80 112	72- 84
\bar{M}_1	175	37 58	30- 36
\bar{M}_2	177	88 122	84- 96
\bar{M}_3	53	143 205	144-192
<i>Root completion—apical closure</i>			
\bar{P}_1	40	134 168	144-156
\bar{P}_2	32	145 184	156-168
\bar{M}_1	87	105 139	108-120
\bar{M}_2	37	154 211	168-180

* Identical ranges given in Kronfeld (4) and Wilkins (2). Values given by Schour and Massler (5) and Arey (6) were obtained by combining maxillary and mandibular "ranges." P, premolar; M, molar.

literature greatly underestimate the variability that exists.

Using serial oblique-jaw x-rays of a total of 255 white Ohio-born participants in the Fels Longitudinal Studies, we determined the time of occurrence of three stages of formation in five mandibular teeth on an individual basis, after reference to each succeeding and each previous x-ray in the series (3). Because of skewness, percentiles were computed, rather than means and standard deviations. Combined-sex distributions were employed throughout.

The 5th and 95th percentiles from the present study were compared with the "ranges" given by Kronfeld (4), which are the basis for the varying values cited in abridged form by other authors (2, 3, 5, 6). As is shown in Table 1, the present 5th to 95th percentile ranges greatly exceed in magnitude the "ranges" previously given, for each of 14 tooth-stage comparisons. On the average, the present ranges and those published by Kronfeld differ by a factor of 3.

There are several possible explanations for the fact that variability of tooth formation as determined here is so much greater than has been accepted hitherto. These possibilities include: the inevitable differences between histological and radiographic approaches; differences in the measure of variability employed; and differences in the populations sampled. However, the most likely explanation lies in the extremely small samples previously investigated. The earlier values are based on a total of 25 to 30 cadavers, most of them from children who were debilitated at the time of death, and many of whom were developmentally abnormal (7). For most of the developmental stages of the teeth here compared, the ranges previously given could not have been based on more than two individuals. In contrast, the present data, though not intended for use as norms, are based on from 32 to 196 examples of each stage of each tooth considered (8).

S. M. GARN

A. B. LEWIS

D. L. POLACHEK

*Fels Research Institute,
Yellow Springs, Ohio*

References and Notes

1. T. D. Stewart and M. Trotter, *Basic Readings on the Identification of Human Skeletons: Estimation of Age* (Wenner-Gren Foundation for Anthropological Research, New York, 1954).
2. L. Wilkins, *The Diagnosis and Treatment of Endocrine Disorders in Childhood and Adolescence* (Thomas, Springfield, Ill., 1950).
3. S. M. Garn, A. B. Lewis, D. L. Polachek, *J. Dental Research*, in press.
4. R. Kronfeld, *The Bur* 35, 18 (1935).
5. I. Schour and M. Massler, *J. Am. Dental Assoc.* 27, 1918 (1940).
6. L. B. Arey, *Developmental Anatomy* (Saunders, Philadelphia, 1957).
7. W. H. G. Logan and R. Kronfeld, *J. Am. Dental Assoc.* 20, 379 (1933).

8. This investigation was supported in part by research grant M-1260 from the National Institutes of Health. We are indebted to Dr. Kalevi Koski for careful analysis of more than 2500 individual x-rays.

24 July 1958

Formation of Metal Alkyls by Ionizing Radiation

Abstract. It has been demonstrated that liquid hydrocarbons, under the influence of gamma radiation, react with "high-surface sodium" to form metal alkyls. The nature of these metal alkyls has been determined, and possible mechanisms for their formation are discussed.

The interaction of alkyl free radicals with metals to form metal alkyls is a well-known reaction. We have found that the irradiation of liquid hydrocarbons in contact with sodium metal supported on aluminum oxide (1) results in the formation of low concentrations of metal alkyls and sodium hydride (2).

Samples of the five saturated hydrocarbons studied were prepared for irradiation by fractional distillation of the best grades of materials available with the final distillation taking place in a vacuum from "high surface sodium." The irradiation vessels were 4.0-ml Pyrex ampoules in which 0.75 to 1.0 g of the "high-surface sodium" (25 percent sodium by weight) had been loaded in a nitrogen-filled dry box. One-gram samples of the hydrocarbons were distilled into the irradiation vessels and degassed thoroughly by repeated freezing, pumping, and thawing cycles. Irradiations were carried out in a 500-c cobalt-60 source having a dose rate of about 3.0×10^{20} ev/lit. min. Carbonation of the samples with $C^{14}O_2$ following irradiation was carried out by the method of Collins (3). The resulting carboxyl-labeled sodium alkanoates were separated by paper chromatography, located on the paper by means of a thin-window Geiger tube, and identified by comparison with the known R_f values for these compounds.

Experimental results relating to the relative yields of the various free radicals captured by sodium are summarized in Table 1. The total dose was 4.0×10^{21} ev for each sample, based on the weight of hydrocarbon in the sample. For the lower hydrocarbons (C_5 or less) the yield of free radicals isomeric to the parent hydrocarbon was about equal to that of the parent. The chromatographic procedure employed did not separate the isomers efficiently above C_5 .

Approximate values of the 100-ev yield of total free radicals captured by sodium are: *n*-hexane, 0.10; *n*-heptane, 0.16; 2-methylpentane, 4×10^{-4} ; 2,2,4-trimethylpentane, 1×10^{-4} . These values are cal-

Table 1. Product radicals (detected as $RC^{14}OONa$) (percentage of total activity)

Parent hydrocarbon	Octyl	Heptyl	Hexyl	Pentyl	Butyl	Propyl	Éthyl	Methyl	H
n-Pentane			3.0	2.0	6.0	2.8	2.0	20	65
n-Hexane			0.5	1.0	0.6	0.4	2.0	41.0	55
n-Heptane	0.5	2.0	10.0	2.0	1.0	1.0	8.5	37.0	36
2-Methylpentane		0.6		1.5			4.0	5.0	86
2,2,4-Trimethylpentane	14.0	6.0	6.0	5.0	17.0	8.0	15.0	23	

culated from the known specific activity of the $C^{14}O_2$ used and from reasonable assumptions about counting efficiency, self absorption, geometry, and other factors. Energy absorption is based on the ferrous sulfate dosimeter yield of 15.6 ferric ions per 100 ev absorbed, with necessary corrections for differences in absorption coefficients. These calculations are based on the energy absorbed in the liquid hydrocarbon only.

The 1000-fold difference in total free radicals originating from the straight-chain hydrocarbons captured by sodium as compared with the branched compounds is possibly in part due to the presence, in the latter compounds, of a tertiary hydrogen atom which would be especially susceptible to attack by the free radicals produced in the bulk of the liquid. This is substantiated by the observation that in the case of both branched compounds the percentage of methyl radicals captured is appreciably lower, and the larger radicals higher, than in the case of the straight-chain compounds, while the over-all yield remains low.

That diffusion rates of the free radicals may also play a role can be inferred from the relative yields (Table 1). In all cases, except 2,2,4-trimethylpentane, the H-atom and methyl yields are much greater than those of any of the larger species produced by radiolysis.

For the highly branched compound, random carbon-carbon scission seems to predominate, while in the case of the straight-chain compounds, the order of susceptibility to breakage is $C_1-C_2 > C_2-C_3 > C_3-C_4$ —that is, a terminal methyl group is most readily removed. This generalization must be tempered, of course, with the observation that the methyl radical may simply have a better chance of being captured and that it thus gives the appearance of being produced in greater abundance. The observation is, however, in general agreement with the results obtained by Gevantman and Williams (4), who used iodine as a free radical trap. These workers found that in the case of ethane, propane, n-butane, and n-pentane, the radicals corresponding to the parent hydrocarbon were not predominant and that methyl radicals represented 25 to 50 percent of the total radical yield, with other small fragments

making up the bulk of the remaining products of the radiolysis.

It is not clear from this study whether or not the reactive species captured are produced on the monolayer of hydrocarbon immediately adjacent to the sodium surface or in the bulk of the system.

RUSSELL H. JOHNSON

ROBERT C. GABLER

Chemistry Department,
Florida State University, Tallahassee

References and Notes

- U. S. Industrial Chemicals Co. Bull. (1953).
- This work was supported in part by a research contract from the U.S. Atomic Energy Commission, and in part by a grant from the Florida State University Research Council.
- C. J. Collins, *J. Am. Chem. Soc.* 70, 2418 (1948).
- L. H. Gavantman and R. R. Williams, Jr., *J. Phys. Chem.* 56, 569 (1952).

24 December 1957

Prolonged Natural Deferment of Hatching in Killifish

Abstract. The drying up of flooded lowlands stranded eggs of *Fundulus confluentus*, which were unhatched and viable after as much as 3 months' exposure. The eggs were found in the moist plant debris on the soil surface. When ovigerous sods were immersed in tap water, normal fish hatched within 15 to 30 minutes.

Under natural conditions, delay in hatching greatly exceeding the minimal incubation period is recorded only of the California grunion (*Atherinidae*) and certain of the Cyprinodontidae in South America, Africa, and India. The eggs of these fishes lie buried in sand (1) or mud (2) or immersed in stagnant water (3), as the case may be, pending onset either of a rainy season or of spring tides, when they hatch. Fundamentals of the hatching mechanism have been worked out experimentally for the Nearctic cyprinodont, *Fundulus heteroclitus* (4), and its hatching has been indefinitely postponed artificially (5). The hatching physiology of the Japanese cyprinodont, *Oryzias latipes*, has been clarified by a series of experiments (6). Since neither species is at present known to undergo a significant delay in hatching in a state of nature, the experimental results have not been examined in an ecological context.

In the autumn of 1957, in Vero Beach,

Florida, eggs of marsh killifish, *Fundulus confluentus* Goode and Bean, were found to remain viable out of water for long intervals, when stranded on the ground surface among plant litter after accumulations of rainfall runoff had dried up. Sods cut during the period 9-18 December from a swale bottom from which the water had disappeared 2 months or more earlier yielded hatchlings 15 to 30 minutes after the sods were immersed in pans of tap water. At the time of hatching, the yolk sac is obsolescent, and the larval fish start feeding as soon as they escape from the chorion. A sod cut from an exposed lowland bottom on 19 September was kept out of water in the shade for 3 months and 5 days and lightly sprinkled once a week. After being immersed in a pan of water on 23 December, it yielded a hatchling fish.

All oviposition sites located by sampling were at the margins of formerly flooded areas, where the eggs would be left stranded by the first contraction of the perimeter of the standing water. Oviposition had been confined to accumulations of fresh water from rainfall runoff, which may have devious temporary connections with nearby brackish waters during the August-September rainy season. However, *F. confluentus* is euryhaline, with a preference for brackish water, and is abundant in regions without access to fresh water, so that it probably oviposits also at the fluctuating margins of brackish tidal waters.

The hardiness of the stranded eggs exposed to the atmosphere is evident from the fact that fry were obtained from the swale on 29 January, after it had been reflooded by heavy rainfall at the beginning of January, following the most sustained cold weather in Florida in over 15 years. These ranged from roughly 2-week to 4-week size, as measured by those reared from the egg in the laboratory. In both field and laboratory, the hatchlings developed normally and rapidly in fresh water (7).

R. W. HARRINGTON, JR.

J. S. HAEGER

Entomological Research Center,
Florida State Board of Health,
Vero Beach

References and Notes

- W. F. Thompson and J. B. Thompson, *Calif. Fish Game, Fish Bull.* No. 3 (1919), pp. 3-29; F. N. Clark, *Calif. Fish Game, Fish Bull.* No. 10 (1925), pp. 1-51; L. R. David, *Copeia*, No. 2, 75 (1939).
- G. S. Myers, *Stanford Ichthyol. Bull.* 2, No. 4, 89 (1942).
- S. Jones, *Current Sci. (India)* 13, 107 (1944).
- P. B. Armstrong, *Biol. Bull.* 71, 407 (1936).
- R. Milkman, *ibid.* 107, 300 (1954).
- J. Ishida, *Annotations Zool. Japon.* 22, No. 3, 137 (1949); *ibid.* 22, No. 3, 155 (1949).
- This report is contribution No. 61 of the Entomological Research Center, Florida State Board of Health. It was supported by research grant RG-5415, National Institutes of Health, U.S. Public Health Service.

28 July 1958

Meetings

International Cancer Congress

Cancer is a relentless enemy of mankind, yet its story is filled with human triumphs as well as suffering. This thought was never too far out of sight during the recent meeting of nearly 2500 cancer research workers from 64 countries, who convened in London from 6 to 12 July for the 7th International Cancer Congress. During the many sessions, symposia, and discussions, the current status of the cancer problem in 1958 gradually evolved in all its fascinating intricacies, uncertainties, and successes.

Theory of Carcinogenesis

In a congress plenary session on carcinogenesis, Sir M. Burnet (Melbourne, Australia) outlined his simple and explicit theory. Cancer cells are derived from normal cells by somatic mutation followed by clonal selection. The somatic mutation must either give the mutated cell an advantage in growth rate or must bring it within one step of such an advantage. Virus particles can cause an equivalent change by adding genetic information to the cell, possibly in a manner similar to bacterial transformation or transduction. Following its initiation, the evolution of the cancer cell clone is a random process of selection similar to Darwin's concept of the evolution of the species.

Burnet illustrated the incidence of somatic mutation in mammals with the story of fleece mosaic. About 30 out of 20 million Australian sheep have varying patches of long wool on their skin, and study indicates that this is due to a somatic mutation occurring at the rate proposed by Burnet as responsible for cancer. Like the theory of Armitage and Doll, Burnet's theory successfully accounts for the age incidence of common types of cancer. Burnet doubted the viral etiology of such cancers.

Physical Carcinogenesis

Physical carcinogenesis, as reported by E. T. and B. S. Oppenheimer *et al.* (New York) is a highly significant development. A thin solid sheet of any material—be it plastic, glass, parchment, mica, or metal—will produce from 5 to 55 percent incidence of malignant tumors (mainly fibrosarcomas) when im-

bedded subcutaneously in rodents. Initially, the sheet causes a rapid growth of fibroblasts around it; this slows up after 3 months and results in a thick pocket of inactive fibroblasts after 6 months. If cancer develops, it starts later, within an occasional isolated patch of reactivated fibroblasts. These patches usually arise near the inner surface of the pocket but may fail to appear. On the other hand, with woven fibers or powders of the same materials, there is often liberal fibroblastic growth, but no true pocket is formed and the tumor incidence is under 1 percent. Thus, the relevant feature is the physical form of the obstructing material. More important, one might deduce that the physical form of the fibroblastic pocket, rather than the mere presence of fibroblastic proliferation, initiates carcinogenesis.

Chemical Carcinogenesis

Chemical carcinogenesis was discussed by C. Heidelberger (Madison, Wis.), who presented evidence for a direct relation between the carcinogenicity and the degree of protein-binding of a skin carcinogen. But I. Berenblum (Rehovoth, Israel) thought that protein binding of the metabolites of a carcinogen may be nonspecific and questioned whether the original compound or a metabolite is the relevant carcinogen. He thought that dissection of the carcinogenic process into an "initiating" and a "promoting" phase has aided precise study, while P. Shubik (Chicago) thought a single-stage process applied.

The possible relation between occupational and spontaneous bladder cancer was highlighted. Bladder cancer was reported in 85 French workers exposed to aromatic amine dyestuff intermediates (J. L. Billiard-Duchesne, Rouen, France), in 16 American workers who had suffered long-term exposure, and in six other American workers who had been briefly or intermittently exposed (W. F. Melick, St. Louis). A better solution than routine cystoscopic examination for such workers is elimination of the manufacture of the responsible carcinogens, which include 2-naphthylamine, benzidine, and xenylamine. According to G. M. Bonser (Leeds, England), the active carcinogens are the orthohydroxy metabolites of these amines.

Such orthoaminophenols are also produced spontaneously in man as normal metabolites of tryptophan, and E. Boyland (London, England) found that some of these are bladder carcinogens in mice. In man, these orthoaminophenols are rapidly conjugated by the liver and excreted in urine. While in the bladder, the inactive glucuronide conjugates are hydrolyzed by β -glucuronidase and thus become free to cause bladder cancer. Boyland found that most men with bladder cancer excrete more such orthoaminophenols and more β -glucuronidase than do normal subjects, and expressed the hope that bladder cancer might be prevented by inhibiting urinary β -glucuronidase with an oral drug. R. R. Brown and J. M. Price (Madison, Wis.), on the other hand, found that about 50 percent of patients with spontaneous bladder cancer had an abnormal tryptophan metabolism, but so also did 50 percent of patients with cancer of other sites. In most patients of both series, this abnormality could be partly corrected by administration of vitamin B₆. Brown thought that certain tryptophan metabolites that appear in human urine may have a causal significance in spontaneous bladder cancer, but other exogenous and endogenous factors are also relevant. In this context, J. Clemmesen (Copenhagen) reported that cigarette smoking is an important additional factor.

Lung Cancer

Lung cancer is the only common type of cancer whose incidence has rapidly increased in recent years. Unanimous agreement regarding certain aspects of this problem was demonstrated by congress lecturers.

L. Kreyberg (Oslo) reported that lung cancer can be divided into two histological groups: group I tumors, comprising mainly epidermoid and undifferentiated carcinoma, with an incidence related to external irritants and especially to cigarette smoking; and group II tumors, comprising mainly adenocarcinoma, with equal incidence in males and females and in rural and urban areas. While W. C. Hueper (Bethesda, Md.) disagreed that the incidence of group I tumors is related to cigarette smoking, W. Haenszel and M. B. Shimkin from the same institute used Kreyberg's classification to show that the incidence of group I tumors in women rises with the amount of cigarette smoking, just as other studies have shown this to be true for men. They found that the incidence of lung cancer in nonsmokers is roughly the same in men and in women. Their results indicate that the main disparities in lung-cancer death rates of men and women are resolved when smoking habits are considered. The authors noted that their study, the largest with female

subjects to date, agreed with the only other three sizable studies of this type so far published.

R. Doll (London, England) reported agreement between the results of his large prospective and retrospective studies: The incidence rate of lung cancer is over ten times as high in the average cigarette smoker as in nonsmokers, and the risk is proportional to the number of cigarettes smoked daily and increases with duration of the habit. For those who have stopped smoking for over 10 years, the rate is one-quarter that for persistent smokers. Similar results were reported by H. F. Dorn (Bethesda, Md.) for a prospective study among 290,000 American men: The incidence rate of lung cancer is over nine times as high in the average cigarette smoker as in nonsmokers, and cigarette smokers have a better chance of avoiding lung cancer if they stop smoking. E. L. Wynder (New York) reviewed his epidemiological studies and the evidence on experimental induction of lung cancer with tobacco smoke. On both counts, he has long since considered cigarette smoking established as the primary cause of lung cancer.

Regarding air pollution as an etiological factor in lung cancer, R. E. Waller (London, England) reported that there is a 2/1 ratio in over-all mortality from lung cancer in large towns as compared with rural areas in Britain. He suggested that part of the difference in lung-cancer mortality between urban and rural areas hitherto attributed to air pollution is only temporary in nature and reflects a later onset of cigarette smoking in the more rural areas. However, the data of P. Stocks (Colwyn Bay, Wales) indicated clearly that the relatively heavy atmospheric pollution in certain British cities is a major factor responsible for this urban-rural difference.

In a symposium on lung cancer, data of E. C. Hammond were quoted which show that the lung-cancer death rate of cigarette smokers in large American cities is five-fourths of that in rural areas. One possible explanation for this difference is that urban atmospheric pollution contributes an extra one-fourth as much risk as cigarette smoking. On this basis, an urban nonsmoker should have one-fourth the lung-cancer rate of an average cigarette smoker, and this fits Hammond's figures. His data show that the lung-cancer rate for nonsmokers in rural areas is very low, about 1/30 that of smokers. These considerations explain the findings of Stocks that lung-cancer rates increase faster with increase in cigarette smoking in rural areas than in cities: the lung-cancer incidence in rural nonsmokers is low enough for habitual smoking of even a few cigarettes to have a marked effect on lung-cancer rates (1).

Experimental evidence on air pollu-

tion was given by Hueper, who cited industrial dusts containing chromates, nickel, arsenic, asbestos, iron oxide, and possibly beryllium as carcinogenic for man. In addition, combustion products from coal, wood, and gasoline are carcinogenic. From these data, from the pathology of occupational lung-cancers, and from consideration of lung-cancer rates in cities in the United States without reference to individual smoking habits, he concluded that atmospheric pollution is a more important factor than smoking, although he agreed that cigarette smoking is a cause of lung cancer. P. Kotin (Los Angeles) concluded from laboratory studies that the environmental carcinogens responsible for lung cancer include polluted atmosphere, infectious agents, and cigarette smoke. L. M. Shabad (Moscow) reported that atmospheric pollution may be one of the causes of lung cancer, and that use of advanced fuel-burning systems and rational city planning can decrease or prevent atmospheric pollution by 3,4-benzopyrene.

Experimental evidence on cigarette smoke was given by P. R. Peacock (Glasgow), who produced lesions of the respiratory tract in domestic fowls after 2 years of directing cigarette smoke thrice weekly into their buccal cavities. J. W. S. Blacklock (London, England) obtained lung tumors in two out of eight rats by inoculating the condensate from cigarette smoke directly into the lung substance. S. Neukomm and J. Bonnet (Lausanne, Switzerland) reported exact figures for the content of the powerful carcinogen 3,4-benzopyrene and of four other aromatic carcinogens in tar from cigarette smoke.

As for the future, J. Clemmesen calculated that if the present trend continues, then by 1990 the male lung-cancer incidence in Copenhagen will equal the 1950 figure for male cancer of all other sites together, and this increase will be due almost entirely to cigarette smoking, since Copenhagen has practically no atmospheric pollution.

The conclusion drawn here is that all investigators reporting epidemiological studies of the effect of cigarette smoking on lung-cancer incidence agreed unanimously that cigarette smoking is the main cause for the present increase in this disease (2). Also, all investigators reporting experimental studies in which cigarette smoke was specifically studied for carcinogenic effects agreed unanimously that cigarette smoke is a carcinogen for man (2). From these two sets of agreements it follows that the papers presented establish decisively that cigarette smoking is a cause of human lung cancer, and, beyond reasonable doubt, that cigarette smoking is the main cause of the present increase in lung-cancer incidence. After smoking, atmospheric

pollution emerged as the most significant carcinogen. Epidemiological reports suggested that its effect is smaller but certainly not negligible, even relative to the powerful effect of habitual cigarette smoking; that, for nonsmokers, the incidence rate of lung cancer is very small in rural areas; and that atmospheric pollution greatly increases this rate.

Radiation

Radiation carcinogenesis was discussed at several symposia. H. S. Kaplan (San Francisco) thought that any tissue injury that leads to a disturbance in normal tissue regulatory mechanism may cause cancer. If the repair mechanism is unable to redress the injury, equilibrium is lost and cancer may result. Kaplan found that cancer may develop in a normal thymus retransplanted into an irradiated thymectomized animal; this suggests that total-body irradiation can have humoral effects. On the other hand, J. Furth *et al.* (Boston) reported that head irradiation is as effective as total-body irradiation in producing pituitary tumors in mice, and that these tumors are mostly adrenotropic, while most spontaneous pituitary tumors are mammatropic. Furth concluded that pituitary irradiation causes a tumorigenic change which might be a mutation but that actual development of the tumor depends on stimuli from pituitary-dependent organs.

A symposium on the carcinogenic risk of radiation, held under the chairmanship of W. C. Moloney (Boston), developed into a round-table discussion of whether a threshold exists for radiation carcinogenesis in man and whether there is a straight-line relationship between radiation dose to bone marrow and incidence of leukemia. Opinions were divided, and the discussion served notice that these questions delineate a major area of future controversy.

W. B. Looney *et al.* (Bethesda, Md.) established a link between Thorotrast administration and the occasional development of a rare type of liver tumor, which had a mean latent period of about 15 years in nine patients, and C. M. Gros *et al.* (Strasbourg) reported another such case. Yet C. Johansen (Copenhagen) found no liver tumors in 250 patients who had received Thorotrast from 10 to 20 years earlier but thought evaluation premature, since he found similar liver tumors late in the life of animals injected with Thorotrast. Lastly, N. Petrov *et al.* (Leningrad) induced osteogenic sarcoma in monkeys by bone-marrow injections of radium bromide.

Hormones

Hormonal carcinogenesis in endocrine-dependent organs, according to Sir C. Dodds (London, England), can be caused by an alteration of the natural

hormone background due to ablation of endocrine organs, application of an active hormone, or inborn abnormalities. O. Mühlbock (Amsterdam) thought the alteration that results in cancer of the "target" organ usually exposes it to an excess of a growth-stimulating hormone (that is, pituitary tropic hormones and sex hormones); thus, excess of a hormone can be carcinogenic for the "target" organ, while deficiency usually causes atrophy but not cancer.

These theories can be tested against experimental results reported at the congress. A. Lipschutz (Santiago, Chile) used mice to confirm his finding that subtotal castration produces tumors in sex organs towards the end of the natural life-span. The carcinogenic effects of long-term injections of large doses of sex hormones were documented by H. Kirkman (San Francisco) for testosterone propionate in the Syrian hamster; by N. Petrov *et al.* for estrogens in monkeys; and by W. U. Gardner (New Haven, Conn.) and R. L. Noble and J. H. Cutts (London, Canada) for estrogens in mice. F. Bielschowsky (Dunedin, New Zealand) noted that when the concentration of thyroid hormone falls below a critical level, increased pituitary secretion of thyroid-stimulating hormone results. If the thyroid cannot respond, the pituitary continues its excess secretion; this results first in goiter and often eventually in cancer of the "target" organ.

Mammary tumors in mice were linked to hormonal, as well as to viral, stimulation. Thus, L. M. Boot and O. Mühlbock (Amsterdam) reported that subcutaneous transplantation of whole pituitaries into mice free from the milk factor caused induction of mammary tumors. R. E. Kavetsky *et al.* (Kiev, U.S.S.R.) found that the release of mammatropic and gonadotropic hormones during the estrus cycle followed a "disturbed" pattern in mice of the high-mammary-tumor strain C3HA. Experimental neuroses caused by running a 5- to 20-volt electric current through the cage floor altered pituitary gonadotropic activity and lowered the age of tumor incidence from 11 to 8 months. J. J. Bittner (Minneapolis) also found evidence for an inherited hormonal pattern associated with mouse mammary cancer and discussed transmission of the milk factor by the male mouse, while H. B. Andervont (Bethesda, Md.) confirmed the occasional spontaneous disappearance of the mammary agent from a mouse of high tumor strain.

Viruses

Viral carcinogenesis was a stimulating field for participants at the congress. A. M. Prince (New Haven, Conn.) reported that cancer induction by Rous sarcoma virus cannot be explained on a

transduction model. P. Vigier (Paris) thought that Rous sarcoma grows in sensitive hosts more by reinfection of cells than by division of infected cells. New viral tumors included a deer fibroma and a superficial tumor in monkeys. C. Friend (New York) reported a new leukemia-like disease of mice and prepared a Formalin-inactivated vaccine that immunized 80 percent of the mice.

S. E. Stewart *et al.* (Bethesda, Md.) reported that a mouse-leukemia agent, after tissue culture for 2 weeks and subsequent inoculation into newborn mice, produced multiple types of neoplasms in from 60 to 100 percent of two different strains of mice. All mice with neoplasms had tumors of the salivary glands, and many had up to eight other types of unusual primary tumors, including sarcomas of the heart, kidneys, and subcutaneous tissues. Mice could be completely protected against the agent by passive immunization with rabbit antisera. R. Latarjet (Paris) found that injection of leukemic tissue extracts into isologous newborn mice accelerates the appearance of leukemia and occasionally results in unusual multiple primary tumors. A Graffi (Berlin-Buch, Germany) confirmed the finding that cell-free extracts of various transplantable mouse leukemias produce a high incidence of myeloid leukemia when injected into newborn mice, while J. Rygård (Copenhagen) demonstrated that phagocytosis is low in leukemic and in newborn mice.

In his abstract, L. Gross (New York) reported the induction of leukemia in up to 50 percent of a low-leukemia strain of mouse by fractionated doses of x-rays. Cell-free extracts of the leukemic tissues were injected into newborn mice of the same strain and caused an 11-percent incidence of leukemia as compared with a 0.5-percent incidence with cell-free extracts of normal tissues. However, the incidence of parotid tumors was respectively 5 and 7.5 percent in the two groups. Gross thought that mice of a low leukemic strain may carry a latent leukemic agent of low pathogenic potential which may induce leukemia in its carrier host when triggered by ionizing radiation. D. Metcalf and R. Buffett (Melbourne and Boston) found that the pathogenesis of lymphatic leukemia induced by radiation in mice of low leukemic strain is similar to that occurring spontaneously in mice of high leukemic strain. These two papers provide experimental evidence for an alternative to Burnet's interpretation—that, although the age incidence of acute leukemia in man is compatible with a viral etiology, such etiology is unlikely, since radiation can induce leukemia.

No slides of electron micrographs were shown to substantiate the claim of A. D. Timofejevsky (Moscow) that extracts of from 40 to 50 percent of vari-

ous human malignant solid tumors contain round virus-like bodies, but an article was available for inspection that contained two pictures of controversial value.

Biochemical Characteristics

The cancer cell was discussed by V. R. Potter (Madison, Wis.), who gave biochemical meaning to the somatic mutation theory of cancer. He thought that mutation of a gene (deoxyribonucleic acid) results in the loss of specific enzyme-forming systems controlling the inhibition of cell division by a negative feedback mechanism. Gene mutations may show up directly as loss or change of enzymes or cell surface antigens, or may involve enzyme-forming mechanisms (ribonucleic acid), with the same final result. Potter thought that no unique over-all enzyme pattern characteristic of cancer tissue had so far been demonstrated, and that the total picture includes electron transport, carbohydrate metabolism, and nucleic acid synthesis.

S. Weinhouse (Philadelphia) thought, in contradiction to Warburg's theory, that there was no respiratory impairment in tumors but noted that tumor cells have a voracity for glucose. While many quantitative differences between normal and tumor tissues exist, no unique differences in pathways of electron or carbon transport or substrate utilization had been demonstrated. He thought that an enzyme activity may be low or absent in specific tumors, but knowledge of the same system in the normal tissue of origin and in other tumors was lacking. This point was illustrated during the congress by the report of G. Weber and A. Cantero (Montreal) that glucose-6-phosphatase activity is absent in Novikoff hepatoma, while Z. Albert *et al.* (Wrocław, Poland) reported its virtual absence in Crocker sarcoma and mammary adenocarcinoma but its presence in a chrysoidin-induced mouse hepatoma.

Among those who presented experimental papers, D. Burk *et al.* (Bethesda, Md.) reported that the majority of clinical cancer chemotherapeutic agents are strong inhibitors of one or both processes of glycolysis and respiration. From this primary inhibition, secondary effects may result, such as deranged nucleic acid and coenzyme synthesis, or cell breakdown and death. Burk found a good correlation between clinical response and metabolic effects and concluded that the method of metabolic analysis presented by him and his coworkers offers a promising new approach to the selection of agents for clinical trial. S. Graff *et al.* (New York) reported on tumor growth inhibition when the acclimatized host is kept under hypoxia. They thought that this inhibition was due to the inability of tumors to become acclimatized, since even under normal oxygen tension the

high glycolytic rate of cancer cells was a consequence of the inadequacy of normally constituted respiratory processes to keep pace with the exorbitant capacity of tumors for replication.

Metabolism

The metabolism of tumors was discussed by P. Emmelot (Amsterdam), who found that the endogenous respiration of ascites tumor cells is mainly due to oxidation of cellular fatty acid, while D. M. Watkin (Bethesda, Md.) noted that there is an increased utilization of body fat in human cancer patients and thought that this is responsible for the negative caloric balance of patients with active cancer. R. E. Greenfield and V. E. Price (Bethesda, Md.) reported that the anemia of tumor-bearing animals is due to blood destruction through vascular lesions in the area of the tumor, while W. Nakahara (Tokyo, Japan) found that tumor depresses the liver catalase activity of its host by interfering with the utilization of iron in the synthesis of catalase. A possible inference from these two papers is that the depression of liver catalase activity in tumor-bearing animals is partly due to a deficiency of iron for catalase synthesis.

In the area of protein synthesis, P. C. Zamecnik *et al.* (Boston) reported that soluble ribonucleic acid is directly involved in the sequence of enzyme reactions leading from free amino acid to protein. The synthetic pathway is similar for normal rat liver and for mouse Ehrlich ascites tumor. H. Busch *et al.* (Chicago) found that synthesis of the histone fraction of nuclear proteins from L-lysine occurs from three to ten times faster in two transplantable tumors than in normal rat tissues. Regarding radiosensitizers, F. Seelich (Vienna) reported that hematoporphyrin and related substances potentiate the action of x-ray on Ehrlich mouse ascites cells in vitro, while hematoporphyrin has a protective effect against a lethal dose of x-ray in vivo.

Transplantation

Transplantation of tumors is vital for biochemical and therapeutic studies. W. B. Patterson (Boston) reported a successful heterotransplant into the cheek pouch of cortisone-treated hamsters of a malignant melanoma excised from a patient who is now without evident tumor. Chemotherapeutic experiments have been run on the heterotransplant to determine its susceptibility to hormones and nitrogen mustard, for reference in case the patient develops metastases. The method is yet of limited application, since in Patterson's study only one-third of the tumors specially selected for high growth potential would take. H. E. Pogossian *et al.* (Moscow) reported use of the steppe lemming for biological experiments. This rodent is somewhat simi-

lar to the mouse, and mouse sarcoma 180 will grow in from 80 to 90 percent after subcutaneous transplantation. Work on inbreeding is in progress.

Tissue Culture

Tissue culture was used by K. K. Sanford *et al.* (Bethesda, Md.) to show that a clone of cells originally derived from one cell of normal subcutaneous connective tissue of a strain C3H mouse can undergo neoplastic transformation in vitro. G. O. Gey *et al.* (Baltimore) noted that human tumor cells respond less easily to tissue culture than do normal lung cells.

Cytology

In the area of cytology, C. E. Ford and R. H. Mole (Harwell, England) reported that while normal tissues show a high degree of chromosomal constancy, with only 1 in about 500 mitoses showing deviation from the normal diploid number of 40, most reticular neoplasms show much less constancy and often have a slightly greater diploid number. From one to six distinctive new chromosomes may be present as a characteristic feature of the chromosome set and remain unchanged through serial passage; this suggests that each is genetically unique. In this connection, B. M. Richards and N. B. Atkin (London, England) found that the ratio of deoxyribonucleic acid content to chromosome number is generally significantly greater in tumors than in normal epithelia.

Immunology

The immunology of tissue antigens is an area in which rapid advances are being made. Since it seems easier to exploit a gain rather than a loss in antigenicity of the cancer cell, the report of L. Sachs (Rehovoth, Israel) was welcome. All homotransplantable tumors that he has investigated have gained antigenicity in comparison with the tissue from which they were derived, irrespective of whether or not they have lost agglutinogens. Regarding loss of antigens, H. N. Green (Leeds, England) thought that cancer results from a cytoplasmic deficiency of a lipoprotein complex which contains the tissue-specific antigen. Similarly, E. Weiler (Pasadena) said that the kidney-specific antigen is lost during carcinogenesis. In contrast, L. A. Zilber (Moscow), working with liver and hepatoma, thought that tumors do not lose their tissue-specific antigen. However, other antigens of normal tissues may be absent in tumors and, conversely, some tumors may contain additional antigens.

Preferential in vivo localization of I^{131} -labeled antibodies in isologous and homologous tumors was reported by D. Pressman and E. D. Day (Buffalo) and by I. L. Spar *et al.* (Rochester). Press-

man concluded that the tumors tested contain identical or cross-reacting antigens which are either absent or present to a very small extent in normal tissues. Regarding the cytotoxic effects of rabbit antisera with respect to mouse lymphoma cells, J. G. Kidd (New York) found enhancement by normal guinea-pig serum; this serum was also effective alone, presumably due to its content of complement. On the other hand, R. Willheim (New York) ascribed the strong cytotoxic effect of normal human serum against mouse Ehrlich ascites cells to properdin, since zymosan abolished the effect.

E. J. Ambrose and G. C. Easty (London, England) showed a fascinating film of cell movements of normal fibroblasts and sarcoma cells in tissue culture, using the new interference microscope. The film showed that normal cells readily form permanent adhesions with their neighbors which restrict their movement, while cancer cells do not, and the latter move freely over normal cells and over each other. The change from normal to tumor cell is accompanied by a decrease in mutual adhesiveness of the cell surface and continues progressively as the tumor becomes more anaplastic. During the change, the cells become progressively more negatively charged. Thus, acquisition of decreased cell adhesiveness and increased negative charge seems to be characteristic of the neoplastic transformation and of tumor progression.

Detection

Since chances for a complete cure are highest while the cancer is still small and localized, L. T. Coggeshall (Chicago) thought the originators of the American Cancer Society acted wisely in 1913 when they fixed as one of their major goals the education of "the public in the absolute necessity of treatment at the earliest indication of cancerous growth." According to G. Pifer (Toronto), more people would seek early diagnosis if cancer education presented the facts of the disease in a positive manner, to popularize a more hopeful attitude towards the disease. M. Donaldson (Oxford, England) concluded that cancer education will save many lives and quoted Emerson's saying that "knowledge is the antidote to fear."

The physician is aided in cancer diagnosis and therapy by receiving specialized training at all professional levels, and by help with respect to provision of adequate physical facilities and specialized equipment. According to N. P. Duany (Havana, Cuba), these vital services depend on the financial resources available in each country for the fight against cancer. He thought a continuous educational campaign should be carried on through lectures, films, symposia, and journals, and that anticancer centers, de-

tection clinics, and cytological laboratories should be set up. It was good to hear from J. R. Heller (Bethesda, Md.) that in the United States these programs are being directly carried out or financially supported through the cooperative efforts of the American Cancer Society and the National Cancer Institute of the U.S. Public Health Service. Perhaps most important, progress is being assured through increasing support of cancer research.

Exfoliative cytology was stressed as being of high life-saving value, because it permits diagnosis of cancer at an early stage. For cancer of the cervix uteri, H. Yagi (Okayama, Japan) reported that a triphenyltetrazolium chloride stain was superior to Papanicolaou's staining method. A diagnostic rate of about 1 in 300 unselected patients was reported by H. C. McLaren (Birmingham, England), which agrees with D. A. Wood's figures for cervical-cancer screening programs in the United States. A. F. Anderson (Edinburgh) reported a rate of 1 in 70 for a group of 1000 patients without symptoms but referred by private practitioners. In achieving maximal diagnostic accuracy, J. E. Ayre (Miami) found that histological confirmation of positive smears was valuable.

For 500 patients with lung cancer, L. V. Ackerman and H. J. Spjut (St. Louis) found that bronchial biopsies were positive only for 28 percent, as compared with positive findings for 60 percent if exfoliative cytology was used and for 80 percent if three or more cytological examinations were made. Cancer cells were often found in pleural washings after incision biopsy; this suggests that tumor cells may have seeded the pleural surface. No diagnostic errors were found to have been made in 48 operations performed on the basis of positive clinical, radiographic, and cytological findings but negative bronchial biopsies. Similarly, D. S. Rome (Albany) reported a diagnostic accuracy of from 65 to 85 percent with exfoliative cytology.

In the cytological examination of gastric washings, J. B. Duguid (Newcastle-upon-Tyne, England) improved to over 90-percent accuracy with experience. He had initial difficulty with cells appearing in chronic atrophic gastritis, which were almost indistinguishable from carcinoma cells. For cytological diagnosis of cancer of the esophagus, O. T. Messelt (Oslo) obtained 90-percent accurate results. G. N. Papanicolaou (New York) believes that exfoliative cytology also shows great promise for diagnosis of cancer of the rectum and bladder and of the pleura and peritoneum.

W. H. Cole *et al.* (Chicago) and G. E. Moore *et al.* (Buffalo) both reported that about 30 percent of patients with disseminated cancer have cancer cells in the peripheral circulation. For "cur-

able" patients, Cole's figure was 17 percent, while Moore's figure was somewhat lower. Both teams of workers found that surgical operation for removal of the cancer sometimes stimulated release of cancer cells. M. Lenz (New York) studied circulation in the tumor bed and concluded that richly vascularized tumor beds are best equipped to spread cancer. He thought that especially wide fields of treatment should be used with cancer growing in richly vascularized tissue.

Surgical biopsy, according to W. Boyd (Toronto) and G. Gricouroff (Paris) must be the means of determining whether a doubtful lesion is a tumor and, if so, whether it is benign or malignant, localized or invasive, operable or inoperable, radiosensitive or not. The role of surgical biopsy as a disseminating factor in cancer of the breast, unless immediately followed by surgical treatment, was clearly documented by C. Sayago and D. Sirebrenik (Santiago, Chile). In a group of 40 cases in which an average delay of 33 days occurred between a positive surgical biopsy and radical mastectomy, the five-year survival rate was 22 percent. In a second group of 40 cases where biopsy was immediately followed by radical mastectomy, the five-year survival rate was 85 percent.

P. B. Hudson (New York) reported an 11 percent incidence of prostatic cancer in a random sample of 800 men above 45. As a result, Hudson strongly recommended treating prostatic enlargements by surgical operations, which are chosen after a frozen-section diagnosis of the posterior prostate has been made. J. S. Lott *et al.* (London, Canada) used small-needle biopsy to prepare cytological smears on albumin-covered slides. The method was useful for breast tumors, secondary lymph-node metastases, and soft-tissue tumors.

While x-ray examination is a most valuable diagnostic tool, the use of chest x-ray screening programs remains controversial. For Norway, where 16 percent of the civilian population is screened each year, H. Høst (Oslo) reported that one new case of primary lung cancer is discovered per 13,000 chest x-rays. This rate of discovery adds up to 10 percent of all new cases, while about 60 percent of these new cases had had at least one mass x-ray examination within the preceding 4½ years. This does not imply that five-sixths of the cases were missed, since most cancers must have enlarged in the interval between x-ray examination and diagnosis.

In the area of clinical laboratory tests for diagnosis of cancer, W. H. Fishman (Boston) reported, from a study of 100 patients, that measurement of the serum acid phosphatase that is sensitive to inhibition by L-tartrate provides the best laboratory indicator for cancer of the

prostate, since the level is often elevated even in nonmetastatic cancer of the prostate. D. W. Molander *et al.* (New York) noted that elevated serum glutamic oxalacetic levels are useful in the diagnosis of hepatitis in icteric patients with lymphomas or other neoplastic disease.

Distribution

Population studies showed that cancer is becoming more common as medical science raises the life-span of man. Thus, V. A. Marcial (San Juan, Puerto Rico) reported that in 1930 the average life expectancy of Puerto Ricans was 40 years and that cancer was the seventh cause of death. Today, the life expectancy is 68 years, and cancer is the second cause of death.

Valuable clues to the causes of "spontaneous" cancer can emerge from studies of cancer distributions in different geographical locations and ethnic groups. J. N. P. Davies (Kampala, Uganda) reported that leukemia is much less frequent in African peoples than in Europeans, while the incidence of lymphomas is higher; this suggests that the etiology of these lesions differs in Africans and in Europeans. Similarly, K. Takeda (Sapporo, Japan) reported a lower rate of leukemia in Japan (about one-third to one-half the rate in Western countries and in the United States) and also an unusually low proportion of chronic leukemias. Regarding differences in cervical cancer rates of different ethnic groups, a cooperative study between J. Casper (Petah Tiqvah, Israel) and L. J. Dunham *et al.* (Bethesda, Md.) showed identical incidence rates in Jewish women living in Israel and in New York. The incidence rates for New York residents from other ethnic groups were four times higher for non-Jewish women, 11 times higher for Negro women, and 23 times higher for Puerto Rican women. The study failed to confirm the theory that lack of circumcision of the male partner is associated with cancer of the uterine cervix.

Therapy

Surgical treatment of cancer was discussed by J. F. Nuboer (Utrecht, Holland), who thought that the recent advances have not resulted from improvement in surgical technique but from the help obtained from the basic sciences. O. H. Wangenstein (Minneapolis) reported experiences with routine "second look" operations, performed at intervals of six months until a negative look is obtained. In 165 patients operated upon for cancer of the stomach, colon, or rectum, one-half still had cancer at the first reexploration; in 11 percent of this group negative findings were eventually achieved after reoperation. In the other one-half—patients who were apparently

Kodak reports on:

your last chance to get a useful but unpopular booklet . . . how much better x-ray film is getting . . . the sort of thing that crowds our catalog

Photoelastic stress analysis

To the man who needs our little booklet "Photoelastic Stress Analysis," it's a real gem. The trouble is that we haven't been able to find many people who need it. Whether we first overestimated the number of persons who want to determine experimentally the relation between the shape of an object and the mechanical stresses within it, or whether we are now underestimating their numbers, they failed to find their way to our booklet among the literature we publish for photographers. We shouldn't have expected them to. Now we are discontinuing it.

If you want a copy, check with your Kodak dealer. If, as we suspect, he doesn't remember anything about it, send 35¢ to Eastman Kodak Company, Sales Service Division, Rochester 4, N. Y. Don't neglect to mention the title.

AA—KK

X-ray film is getting better.

Our fastest kind used to be *Kodak Industrial X-ray Film, Type K*. Now we call it *Type KK*. The speed has gone up 50%. A 72-hour exposure becomes a 48-hour exposure. Time

is money. So they say. Same principle applies to uranium fuel elements. (To Cs^{137} gamma rays, $\frac{3}{4}$ " of uranium looks like 4" of steel.) *Type KK* is a bit grainier than *Type K*. But it has higher contrast. The gain outweighs the loss. Up goes "radiographic sensitivity."* Radiographers can spot smaller voids.

Kodak Industrial X-ray Film, Type AA beats *KK* seven ways to Sunday for "radiographic sensitivity." It's some slower, though. As *Type A*, it used to be a lot slower. That was a little over a year ago. It was then the most widely used x-ray film in industry. Now it's more so. That sounds like tautology. Nevertheless, it makes us happy. With the higher speed, inherent contrast has gone up, not down. Grain's the same. This is remarkable.

They can just reduce exposure time. Even for thinner specimens, time is money. So it is said. Or they can cover more area at a single exposure. That's another way to save time.

Or they can take the same time and get more film density. Contrast

*Don't trip. "Sensitivity" doesn't mean "speed" here.

and therefore "radiographic sensitivity" improve at higher density.

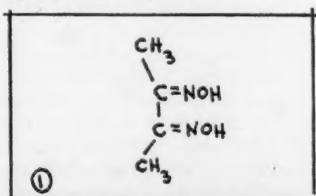
Or they can get through the specimen with less penetrating radiation. Softer radiation emphasizes density differences along ray paths of slightly different absorption. You want those differences.

Kodak Industrial X-ray Film, Type M is for maximum detail and no rush, or else light specimens. *Kodak Industrial X-ray Film, Type F* goes with calcium tungstate screens. Their fluorescence in the visible intensifies the exposure. In a pinch that's sometimes all right.

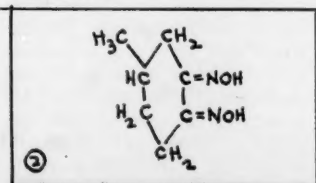
Don't worry. You'd get the hang of it if you had to. Yes, even the radiography of plutonium hardware, where you're recording both endogenous and exogenous radiation. We'd give you what advice we could (but very little about plutonium). You'd write Eastman Kodak Company, X-ray Division, Rochester 4, N. Y.

We also have some freshly minted advice on silver-sensitized goods for dosimetry, including a bibliography. If that's all you want, write Eastman Kodak Company, Special Sensitized Products Division, Rochester 4, N. Y. Ask for the new pamphlet, "Radiation Monitoring with Kodak Personal Monitoring Films." It's useful for processing techniques, if nothing else.

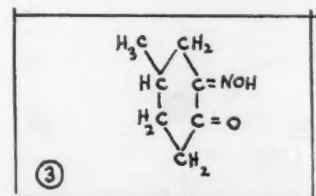
The isonitroso that wasn't expected



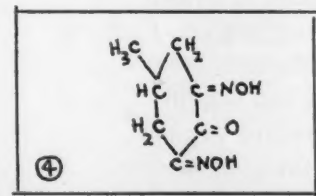
Dimethylglyoxime (Eastman 98), a rip-roaring success as a nickel reagent. Precipitate so beautiful that it's used in the lipstick trade.



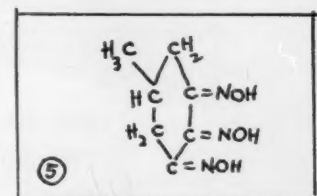
Reported recently by some fellows as an improvement. We want to make it, but we hate to mess around with selenium dioxide the way they did.



What we hoped to get reacting 4-Methylcyclohexanone (Eastman 3083) with iso-Amyl Nitrite (Eastman 436). It's common knowledge that an alkyl nitrite will isonitrosate a methylene adjacent to a carbonyl.



What we actually got. Nature appears to be bent on isonitrosating next to a carbonyl group, even at the expense of leaving some of the original ketone unreacted in case of insufficient nitrite.



Ketonic carbonyl oximated, by hydroxylamine. This part of the plan worked. We have put this in stock as 5-Methyl-1,2,3-cyclohexanetrioxime (Eastman 7478). We hope somebody will discover what it is a reagent for.

One of these years we are going to have to consider smaller print for our catalog, "Eastman Organic Chemicals, List No. 41." Even now there are some 3700 highly purified organics under its covers and in our stockroom. If you don't have a copy, write Distillation Products Industries, Eastman Organic Chemicals Department, Rochester 3, N. Y. (Division of Eastman Kodak Company).

This is another advertisement where Eastman Kodak Company probes at random for mutual interests and occasionally a little revenue from those whose work has something to do with science

Kodak

without cancer at the time of reexploration—21 percent eventually died of cancer. The salvage rate of 5.5 percent for the whole group was offset by an equal mortality rate for the "second look" operations; however there were no deaths in cases declared negative on the first reexploration. Wangenstein concluded that the program has shown clearly how extensive the primary operation should be.

For carcinoma of the corpus uteri, W. Hawskworth (Oxford, England) reported an operability rate of 88 percent and a five-year survival rate of 64 per-

cent; the nodes of the lateral pelvic walls are a common site for recurrence. R. M. Fawzy (Cairo, Egypt) noted that bladder cancer comprises 40 percent of cancer in Egypt, possibly because of predisposition to infestation by *Bilharzia*; the operability rate is under 10 percent, with a five-year survival rate of 30 percent. R. Schade (Newcastle-upon-Tyne, England) thought that carcinoma of the stomach develops nearly always in a diseased gastric mucosa and especially in association with chronic atrophic gastritis.

Radiation therapy of cancer, accord-

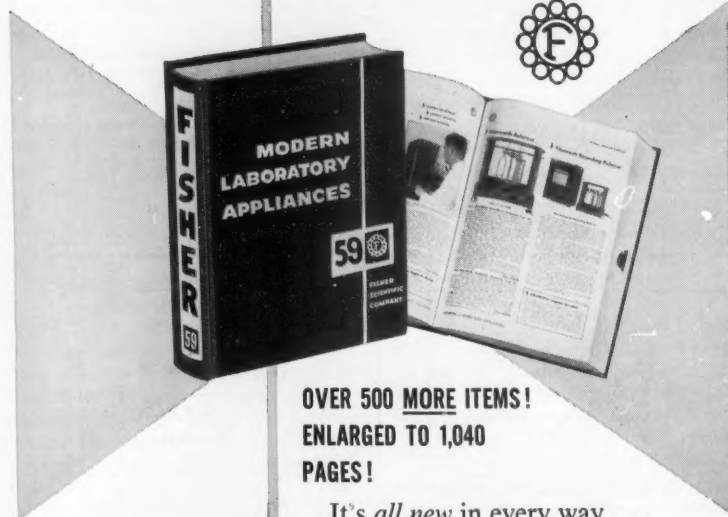
ing to F. Baclesse (Paris) has been improved to deliver an increased dose of radiation to the tumor. This is achieved by physical means, such as rotation, convergence, or grill therapy, and by biological means such as dose fractionation, and high voltage sources are valuable. For conventional x-ray therapy of lung-cancer patients with tumor doses up to 5000 r, S. Mustakallio (Helsinki) reported a five-year survival rate of 2 percent in patients with advanced disease and of 26 percent in a small proportion (3 percent) selected for surgery and postoperative x-ray treatment. L. Larsson *et al.* (Stockholm) found that colloidal Au¹⁹⁸ is taken up by bone marrow only in places of active hematopoiesis. Use of an automatic scanning scintillation counter to obtain bone marrow scintigrams gave valuable information in treatment of chronic leukemia, bone marrow carcinosis, and polycythemia vera.

Endocrine management of cancer of the thyroid has shown spectacular progress, as summarized in exhibits by E. E. Pochin and K. E. Halnan (London, England), L. G. Larsson (Stockholm), and J. C. McClintock (Albany). The therapist has now at his command the surgical techniques of lobectomy, total thyroidectomy, and radical neck dissection, which can be followed by external irradiation. In metastatic thyroid carcinoma, radioiodine often greatly prolongs life; temporary administration of antithyroid drug may revive the functional activity of the tumor and thereby renew its uptake of radioiodine; thyroid hormone sometimes causes regression of hormone-dependent tumors; and external radiation helps to relieve pain.

For disseminated cancer of the breast, R. A. Huseby (Denver, Colo.) reported that adrenalectomy or hypophysectomy benefited one-third of the cases. He stressed the need for a method to predict the results of these operations and noted that for women who are menstruating regularly, failure to respond to castration often heralds failure to respond to androgens, to adrenalectomy, or to hypophysectomy. X-ray treatment and intracavitary colloidal Au¹⁹⁸ are valuable, even for patients already on hormone therapy. Sir C. Dodds (London, England) reported that 30 percent of patients with disseminated breast cancer responded to ovariectomy; he questioned use of hypophysectomy because of high operative mortality. C. Huggins (Chicago) reported that 11 different procedures induce remission in hormone-dependent metastatic cancer of the breast. In two studies on hypophysectomy of patients with advanced lesions, the five-year survival rates were 0 and 4 percent, respectively. Huggins further developed the method of H. Shay *et al.* (Philadelphia) and induced hormone-dependent mammary tumors rapidly in a high percentage

all new...in every way...
not just a revised
edition...

NOW READY... FISHER CATALOG 59



OVER 500 MORE ITEMS!
ENLARGED TO 1,040
PAGES!

It's *all new* in every way . . .
NOT just a revised edition!
528 more items . . . 1,040
pages . . . in **COMPACT**
easy-to-handle size. *More*
illustrations and helpful
reference material . . . the
key source for your labora-
tory needs!

Most comprehensive, complete catalog ever . . . easy to read, easy to use . . . current, up-to-the-minute data. If your laboratory hasn't received its free copy, write today:

139 FISHER BUILDING
PITTSBURGH 19, PA.



FISHER SCIENTIFIC

America's Largest Manufacturer-Distributor of Laboratory Appliances & Reagent Chemicals

IN THE U.S.A.

Boston
Buffalo
Charleston, W.Va.

Chicago
Cleveland
Detroit
New York

Philadelphia
Pittsburgh
St. Louis
Washington

IN CANADA

Edmonton
Montreal
Toronto

B-57b

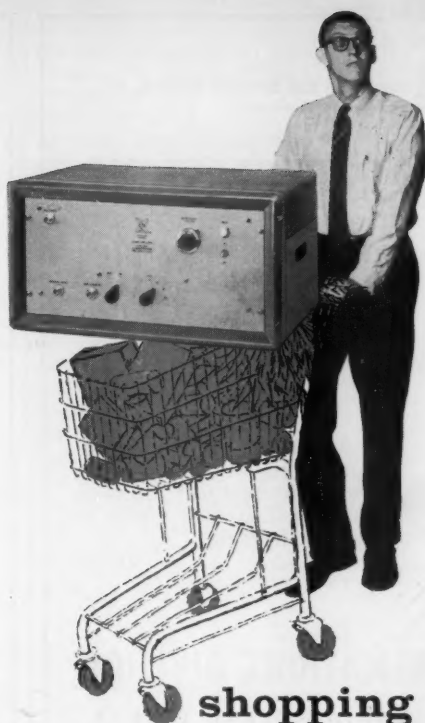
of female rats with a single dose of 5 mg of methylcholanthrene, given by stomach tube; both Shay and Huggins used such tumors to assay hormonal and therapeutic agents.

Chemotherapy

Chemotherapy of cancer, according to T. Yoshida (Tokyo), is taking its place beside surgery and radiation as a unique weapon to prevent metastases and alleviate disseminated cancers. The five main classes of active compounds discussed were alkylating agents, nucleic and folic acid antagonists, quinones, antibiotics, and steroids. One rationale is to poison the cancer cell selectively, by exploiting the very differences that give it a biological advantage.

Nitrogen mustard, with the formula $\text{CH}_3\text{—N—}(\text{CH}_2\text{—CH}_2\text{—Cl})_2$, often abbreviated to HN2, inhibits cell division by reacting with nucleoprotein but produces violent nausea. The less toxic and more soluble phenylbutyric acid derivative Chlorambucil was found to be superior for treatment of lymphocytic leukemias and lymphomas, in Europe and in the United States. Another amino acid (phenylalanine) derivative of HN2 named Sarcolysin was synthesized later independently in the Soviet Union and in England. N. Blokhin (Moscow) reported that Sarcolysin is effective for metastatic seminoma of the testicles but not for metastatic teratoma. Other HN2 derivatives mentioned include the HN2 mannitol compound Degranol, which gives regressions in metastatic cancer (P. Rubányi, Budapest); the N'O-propylene phosphate ester diamide of HN2 named "B-518," which has low toxicity and gives good remissions in lymphosarcomas (R. Gross and K. Lambers, Marburg, Germany); and several others, including drugs showing promise in animal experiments, such as the three-stage drugs formed by linking a two-stage HN2-amino acid derivative like Sarcolysin with another amino acid, vitamin, or nucleic acid precursor (L. F. Larionov, Moscow). Alkylating agents other than HN2 and its derivatives include Myleran, which is effective in treatment of generalized myeloid leukemia or in the radiation-resistant disease (D. A. G. Galton and P. E. T. Hancock, London, England); and *dl*-diepoxybutane, which shows promise in Hodgkin's disease (J. Bichel, Aarhus, Denmark).

C. P. Rhoads (New York) thought that cancer is a somatic mutation which causes changes in nucleic acid structure, and that these changes are the key to the peculiar properties of the cancer cell. Many chemotherapeutic compounds act by interfering with nucleic acid metabolism. Thus, 8-azaguanine is rapidly incorporated into tumor to form a non-functional ribonucleic acid molecule, while, according to P. Feigelson and J. E. Ultmann (New York), it also inter-



shopping for a non-overload linear amplifier?

Our new Detectolab* DA8 is an off-the-shelf instrument which we've been told is an extremely welcome addition to the field of general spectroscopy... or even as our friend Sherman succinctly puts it... specific spectroscopy.

Higher amplifier gain, resolution, linearity and overload factor are but a few features which set this instrument above currently available models.

Overload factor is 4000 times with 7 microsecond recovery rate, making the DA8 especially applicable for use with larger radiation detectors. Additionally, amplifier gain is 70,000, either positive or negative output pulse to 135 v and linearity better than 0.1%. Resolution is 1.0 microsecond.

The Detectolab DA8 permits ready observance of low energy x-rays in the presence of energetic gamma radiation and is available with pre-amp and pulse height selector.

A new technical bulletin excruciatingly describes all aspects of the DA8. Yours for the asking.



BJ ELECTRONICS
BORG-WARNER CORPORATION

Reliability you can count upon
*Borg-Warner Corporation Trademark

3300 NEWPORT BOULEVARD, P. O. BOX 1679, SANTA ANA, CALIFORNIA
EXPORT SALES: BORG-WARNER INTERNATIONAL CORP., CHICAGO, ILLINOIS

Completely rewritten and brought up-to-date

NUCLEAR EXPLOSIONS AND THEIR EFFECTS

RELEASED AUGUST 1958

Press
opinion



"A valuable and dispassionate account of a supremely important subject, suitable for anybody who wants to inform himself".

NATURE

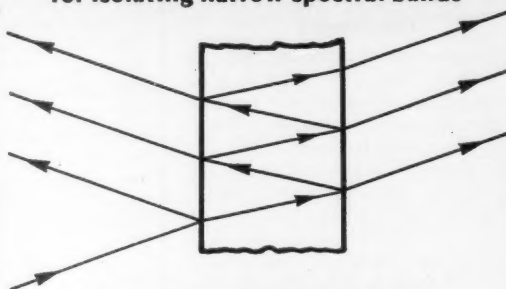
THE PUBLICATIONS DIVISION

OLD SECRETARIAT DELHI (INDIA)

DA-58/203

INTERFERENCE FILTERS

for isolating narrow spectral bands



Spectral Range: 340-900 millimicrons

Peak Transmission: 40%

Half Peak Width: 8-12 m μ

Size: 2" x 2"

For

Colorimetry
Fluorimetry
Flame Photometry

also microscopy, photomicrography, microcolorimetry, refractometry, polarimetry, light scattering measurements, and for many other applications requiring monochromatic light in the visible, near-ultraviolet, and near-infrared range.

Write for Bulletin #180 to

PHOTOVOLT CORP.

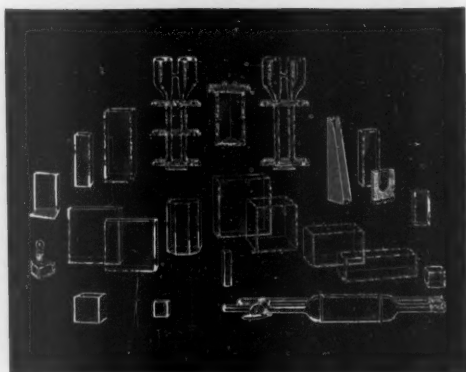
95 Madison Avenue

New York 16, N.Y.

GLASS ABSORPTION CELLS

made
by

KLETT



SCIENTIFIC APPARATUS

Klett-Summerson Photoelectric Colorimeters—
Colorimeters—Nephelometers—Fluorimeters—
Bio-Colorimeters—Comparators—Glass Standards—Klett Reagents.

Klett Manufacturing Co.

179 East 87 Street, New York, New York

FOR EXPLORING
MICROWAVE OPTICS . . .

CENCO® MICRO-WAVE APPARATUS

A valuable new teaching aid for school and laboratory that demonstrates principles of physical optics at a meter stick rather than microscope level. Also illustrates basic radar. Special manual outlines 17 experiments. Write for details.



No. 80422 Micro-Wave Apparatus, with transmitter tube. each \$295.00



CENTRAL SCIENTIFIC CO.
1718-N Irving Park Road • Chicago 13, Illinois
Branches and Warehouses — Mountainside, N. J.
Boston • Birmingham • Santa Clara • Los Angeles • Tulsa
Houston • Toronto • Montreal • Vancouver • Ottawa

feres with nucleic acid metabolism by *in vivo* inhibition of xanthine catabolism. Similarly, C. Heidelberger reported that 5-fluorouracil and related analogs form nonfunctional (or "fraudulent") nucleic acids and also inhibit nucleic acid biosynthesis. A. R. Curreri (Madison, Wis.) found that 5-fluorouracil is clinically effective against tumors but also affects rapidly growing normal tissues, while R. Duschinsky *et al.* (Nutley, N.J.) had synthesized its riboside and deoxyriboside in the hope of reducing toxicity. J. R. Fountain (Leeds, England) found 6-mercaptopurine very useful for chronic myeloid leukemia, perhaps due to activation at a site other than tumor (E. J. Sarcione and L. Stutzman, Buffalo). E. Frei *et al.* (Bethesda, Md.) found 6-azauracil too neurotoxic, while A. D. Welch *et al.* (New Haven, Conn.) reported that its riboside is from 10 to 20 times as effective against mouse tumors. S. Farber (Boston) noted that antifolates act by inhibiting cofactors essential for biosynthesis of nucleic acid precursors and stressed the use of Aminopterin (4-aminopteroylglutamic acid) for acute leukemia in children and of the related Methotrexate for acute leukemia with lung metastasis.

Among quinones, the ethyleneiminoquinone "E-39" inhibits cell glycolysis (N. Gerlich and H. J. Wolf, Bielefeld, Germany) and often gives satisfactory remissions in metastatic cancer and chronic lymphomas (Wolf and Gerlich; J. Bernard *et al.*, Paris). Both Farber and C. T. C. Tan *et al.* (New York) reported favorably on use of actinomycin D with Wilms' tumors; Tan also had good results in children with neuroblastomas but not in adults with metastatic neoplasms. Steroid therapy in chronic lymphatic leukemia was stressed by B. R. Scott (London, England) and by J. G. Freymann and J. B. Vander (Boston); they noted especial benefit in the presence of severe and refractory anemia, but infections were a serious complication.

Ideally, all screening of compounds for cancer chemotherapy should be done in man (C. C. Stock, New York). Since this is impracticable, Stock thought that assay systems such as heterologous transplants of human tumors; spontaneous, induced, and transplantable animal tumors; and tissue cultures and cultures of microorganisms all have their place. With K. Sugiura, he used a new transplantable mouse-virus leukemia to screen 100 different compounds by the simple initial criterion of spleen weight in treated and control mice. R. Bather (Edinburgh) employed day-old chicks injected with Rous sarcoma virus to test antifolates, while A. Goldin *et al.* (Bethesda, Md.) used an advanced mouse leukemia as a rapid assay system.

For objective clinical evaluation of chemotherapeutic response, E. Paterson

(Manchester, England) defined a remission as the time interval after treatment within which a clinical index had again risen to its pretreatment value. The index was calculated by assigning a score of 2 for improvement, 1 for unchanged condition, and 0 for advancing disease to each of ten clinical indications: superficial nodes, mediastinum, spleen, liver, effusions, hemoglobin, fever, well-being, weight, and ability to work. Using this method, Paterson showed precisely how the length of the remission decreased with each additional course of therapy in Hodgkin's disease.

Combination therapy of chemotherapeutic agents with x-rays was reported to give beneficial effects in Hodgkin's disease but not in leukemia (L. Heilmeyer, Freiburg, Germany). Several papers reported effective use of chemotherapy as an adjunct to surgery. L. F. Larionov thought that the antitumor effect of chemotherapeutic substances is inversely proportional to the mass of the tumor, hence that chemotherapy should be more effective when the tumor mass is small—a concept similar to that of Shimkin and Moore. Larionov reported that 18 patients were given HN2 or Novdembichin at an early stage of Hodgkin's disease: 50 percent survived for 5 years; 22 percent, for over 8 years.

Conclusion

In summary, a brief glimpse at the world-wide problem of cancer in 1958 is frankly heartening, showing steady advances on a widening front. Many speakers held that a single cure for cancer is unlikely and studied each group of cancers almost as a separate disease. Some hoped that cancer can be eradicated without an understanding of its very nature; others felt that we must understand better the enigma of the cancer cell and even of life itself. If the somatic mutation theory of cancer is right, then development of cancer is an inherent property of life, and cancer research is but in its lusty infancy. There is every hope that there will be continuing advances in understanding, detection, and therapy.

Thanks are due the British Organizing Committee for its excellent conduct of the congress and for its selection of the pleasant Royal Festival Hall and London County Hall as meeting places. The daily round of entertainments served to make the meeting truly memorable; these included a performance of Aida at Covent Garden Opera House, a delightful garden party at Hurlingham after a boat trip up the Thames, and a performance of the resplendent Guards bands under floodlights at Hampton Court palace.

At the closing session, V. R. Khanolkar (Bombay) was announced as president of the International Union Against Cancer, and A. Haddow (London, Eng-

Important books in NUCLEONICS— PHILOSOPHICAL LIBRARY

- ☐ **ATOMIC ENERGY IN AGRICULTURE** by William E. Dick. A thorough survey of the progress made in this new field of research. \$6.00
- ☐ **ATOMIC ENERGY IN MEDICINE** by K. E. Hahn. A detailed examination of the contribution nuclear physics has made to contemporary medicine. \$6.00
- ☐ **ECONOMICS OF ATOMIC ENERGY** by Mary S. Goldrip. The first major contribution to this important theme. \$6.00
- ☐ **A GUIDE TO NUCLEAR ENERGY** by R. F. K. Bechem. For technical and commercial staffs in the field of power production. This book makes clear to persons with a limited knowledge of physics how nuclear reactors function, describes the more important types being constructed or planned, and surveys the construction materials vital to the nuclear energy industry. Illustrated. \$3.75
- ☐ **NUCLEAR REACTORS FOR POWER GENERATION** Edited by E. Spenshaw Taylor. This book provides an up-to-date survey of the most important aspects of nuclear power generation. A symposium by leading nuclear engineers. Over 50 illustrations. \$7.50
- ☐ **THE ATOM AND THE ENERGY REVOLUTION** by Norman Lansell. The momentous impact of atomic energy on the world's economy, life and society. Chapters discuss the demand and sources of energy; also its exploitation on a national and international level. Illustrated. \$6.00
- ☐ **RADIOACTIVITY MEASURING INSTRUMENTS: A GUIDE TO THEIR CONSTRUCTION AND USE** by M. C. Nokes. This book shows how instruments of fair accuracy can be made in little time and with a minimum of expense. More complicated circuits are included for those who wish to make a simple scaler or recent counting devices. The author is staff member of the Isotope Division of The British Atomic Center, Harwell. Illustrated. \$4.75
- ☐ **THE DIRECTION OF RESEARCH ESTABLISHMENTS.** A timely symposium by 20 American, British, Canadian, Dutch, and German authorities on basic and applied research, budgets and administrative controls, and other problems connected with the organization of research establishments. \$12.00
- ☐ **REASON AND CHANCE IN SCIENTIFIC DISCOVERY** by R. Taton. Dr. Taton examines the relative role of active purpose and chance in the processes of scientific discovery. Steering clear of theory, he illustrates his thesis by practical examples from the work of such scientists as Poincaré, De Broglie, Galileo, Boentgen, the Curies, Leibniz, Newton and others. Illustrated. \$10.00
- ☐ **AN ENCYCLOPEDIA OF THE IRON & STEEL INDUSTRY** by A. K. Osborne. Provides a concise description of the materials, plant, tools and processes used in the Iron and Steel and closely allied industries from preparation of ore to the finished product. Defines all technical terms employed. \$25.00
- ☐ **POCKET ENCYCLOPEDIA OF ATOMIC ENERGY** by Frank Gaynor. More than 2,000 entries defining and explaining concepts and terms in nuclear physics and atomic energy make this volume a vital handbook for all those concerned with atomic science. Illustrations, Charts, Tables. \$7.50
- ☐ **CASTILLA'S SPANISH AND ENGLISH TECHNICAL DICTIONARY.** An unusually complete and up-to-date handbook for all requiring the technical, commercial and legal Spanish-English equivalents. Emphasis is placed on terms relative to currently developing industrial and scientific fields. Two volumes. 2760 pages. \$45.00
- ☐ **PHILOSOPHY OF ATOMIC PHYSICS** by Joseph Mudry. This work promulgates a new philosophical schema, Dialectical Atomism, extending from the primordial era of atoms to a generalized field of extension encompassing the macroscopic order. The author lends challenge and perspective to such topics as: the origin of space and time; the new concept of relativity; entropy and cosmological cycles; our views of immortality; and the meaning of values. \$3.75
- ☐ **OUT OF MY LATER YEARS** by Albert Einstein. The distinguished physicist deals with the most urgent questions of modern society: Social, religious, educational, and racial relationships. Various sections deal with personal credos, politics, education, the Jewish issue, war and peace, the fundamental principles of physics. The author also explains his theory of relativity in simple terms. A treasury of living thoughts by one of our most eminent contemporaries. \$4.75

MAIL THIS COUPON TODAY

Mail to your favorite bookseller or directly to
PHILOSOPHICAL LIBRARY, Publishers
 15 East 40th St., Dept. 10-S-12, New York 16, N.Y.
 Send books checked. To expedite shipment I enclose remittance \$.....
 NAME
 ADDRESS

land) as president-elect. The next International Cancer Congress will be held in the Soviet Union in 1962. In his closing speech the president of the present congress, Sir S. Cade, noted with pleasure the number of young scientists who had attended, saying he thought it augured well for the future.

ARNOLD E. REIF

Department of Surgery,
Tufts University School of Medicine,
Boston, Massachusetts

Notes

1. Application of Doll's findings of proportionality to Hammond's data suggests that smoking four cigarettes per day (about one-fourth the average cigarette consumption) will equal in effect the atmospheric pollution experienced in an average American city. It will therefore increase eightfold the low lung-cancer rate of rural nonsmokers, while doubling the rate for urban nonsmokers.
2. Checked by correspondence following the congress with authors of papers where any possible doubt of agreement existed.

Forthcoming Events

December

29-30. National Council of Teachers of Mathematics, New York, N.Y. (M. H. Ahrendt, NCTM, 1201 16 St., NW, Washington 6.)

29-17. Bahamas Surgical Conf., 1st, Nassau, Bahamas. (B. L. Frank, 1290 Pine Ave., W., Montreal, Canada.)

January

6. Society for Applied Spectroscopy, New York, N.Y. (P. Lublin, Sylvania Research Laboratories, Bayside, N.Y.)

7-9. Northeastern Weed Control Conf., 13th annual, New York, N.Y. (E. R. Marshall, Carbide & Carbon Chemical Co., New York, N.Y.)

12-14. Reliability and Quality Control, 5th natl. symp., Philadelphia, Pa. (W. T. Sumerlin, Philco Corp., 4700 Wissahickon Ave., Philadelphia 44.)

18-31. Bahamas Serendipity Session, Nassau, Bahamas. (B. L. Frank, 1290 Pine Ave., W., Montreal, Canada.)

20-22. American Mathematical Soc., annual winter, Philadelphia, Pa. (E. G. Begle, Leet Oliver Hall, Yale Univ., New Haven, Conn.)

21-22. American Group Psychotherapy Assoc., 3rd annual institute, New York, N.Y. (C. Beukenkamp, Public Relations Chairman, 993 Park Ave., New York 28.)

22-23. Mathematical Assoc. of America, 42nd annual, Philadelphia, Pa. (H. M. Gehman, MAA, Univ. of Buffalo, Buffalo 14, N.Y.)

23-24. American Group Psychotherapy Assoc., 16th annual conf., New York, N.Y. (C. Beukenkamp, Public Relations Chairman, 993 Park Ave., New York 28.)

23-24. Reproductive Physiology and Protein Nutrition, 15th annual conf. on protein metabolism, New Brunswick, N.J. (J. H. Leatham, Rutgers Univ., New Brunswick, N.J.)

24-29. American Acad. of Orthopedic

Surgeons, Chicago, Ill. (C. L. Compere, 720 N. Michigan Ave., Chicago, Ill.)

26-29. American Meteorological Soc., New York, N.Y. (K. C. Spengler, AMS, 3 Joy St., Boston 8, Mass.)

26-29. American Soc. of Heating and Air Conditioning Engineers, 65th annual, Philadelphia, Pa. (W. M. Vidulich, ASHACE, 62 Worth St., New York 13, N.Y.)

26-29. Institute of the Aeronautical Sciences, 27th annual, New York, N.Y. (IAS, 2 E. 64 St., New York 21.)

26-30. Writing and Publication in Industry, conf. and workshops, Brooklyn 1, N.Y. (T. L. Donahue, Writing and Publication Conf., Polytechnic Inst. of Brooklyn, 333 Jay St., Brooklyn 1.)

27-30. Society of Plastics Engineers, Inc., 15th annual tech. conf., New York, N.Y. (L. A. Bernhard, SPE, 65 Prospect St., Stamford, Conn.)

28-29. Nuclear Fuel Elements, 1st intern. symp., New York, N.Y. (H. H. Hausner, 1st intern. Symp. on Nuclear Fuel Elements, 730 Fifth Ave., New York 19.)

28-31. American Physical Soc., annual, New York, N.Y. (E. R. Fitzgerald, Dept. of Physics, Pennsylvania State Univ., University Park.)

29-31. Western Soc. for Clinical Research, 12th annual, Carmel-by-the-Sea, Calif. (W. N. Valentine, Office of the Secretary, Univ. of California Medical Center, Department of Medicine, Los Angeles 24.)

(See issue of 21 November for comprehensive list)

Tachistoscope Projector



P-527 Tachistoscope Projector used to observe the time rate and time condition for apperception, speed of recognition, or any similar situation calling for momentary exposure of visual material.

The projector will accommodate all 2" x 2" slides; 35 mm, Bantam 828 and super slides 1 1/2" x 1 1/2" intermixed if desired.

- 300 watt lamp
- 110 V.—60 cycles
- Illuminated control panel
- Front elevating device
- 4" f/3.5 projector lens
- Magnified slide index window
- 40-slide tray and case

Shutter speeds from 1 sec. through 1/1000. Shutter removable from projector and easily replaced.

P-528 Flashing Shutter, same as above, will fit 2 1/4" diameter lens focusing tube.

PHIPPS & BIRD, INC.

Manufacturers & Distributors of Scientific Equipment



6th & Byrd Streets - Richmond, Va.

Equipment

The information reported here is obtained from manufacturers and from other sources considered to be reliable. Science does not assume responsibility for the accuracy of the information. A coupon for use in making inquiries concerning the items listed appears on page 1526.

■ **TEMPERATURE-CALIBRATING BATH** is a double unit permitting calibration at two temperatures. Temperatures are adjustable from 6° to 260°C above room temperature and are maintained $\pm 0.2^\circ\text{C}$. The inner shell is 10 in. in diameter and 15 in. deep. (American Instrument Co., Dept. 518)

■ **BAR-GRAPH OSCILLOSCOPE** displays 40 channels of telemetered data. Three types are available: a polarity-indicating, low-level d-c system, a wide-band a-c system, and a phase-sensitive a-c system. The bar graph is displayed on a 17-in. cylindrical-face cathode-ray tube. The cylindrical face facilitates use of transparent printed overlays. Parallax error is less than 2 percent for the worst case of observation from the side and is generally less than 0.5 percent. Display errors are less than 1 percent of full scale. Display rate is 10 frames per second. (International Telephone and Telegraph Corp., Dept. 519)

■ **COUNTER-TIMER** is combined with high-and-low count limit setting circuitry to provide limit monitoring of measurands that are convertible into electrical pulse rate. Time bases for pulse frequency measurement are 0.1 and 1 sec. Display time is adjustable between 0.1 and 10 sec. Frequency range as a straight frequency counter is 1 to 100,000 cy/sec. Accuracy is ± 1 count \pm stability. For the standard instrument, stability is determined by power-line frequency stability. A crystal-controlled time base is available to provide stability of 10^{-6} short term and 5×10^{-6} long term. (Computer Measurements Corp., Dept. 522)

■ **FUME-HOOD SASH CONTROL** frees the user's hands entirely for handling reagents and instruments. Sash opening and closing is controlled by a tread. The hood closes automatically when the user walks away. An overriding manual push-button control permits the sash to be moved to any position, and a stop button can be used to halt automatic motion. A third mode of operation permits opening or shutting in case of power failure. (Laboratory Furniture Co., Inc., Dept. 525)

■ **MULTIPLIER PHOTOTUBE** is a nine-stage tube designed especially for detection and measurement of ultraviolet radiation. The tube envelope has a fused-silica section that transmits down to below 2000 Å. Spectral sensitivity at 2000 Å is



for
RESEARCH
in

**MICROBIOLOGY
and TISSUE
CULTURE**

The following Schwarz Preparations are available to assist and extend studies in metabolic and enzymic functions:

ADENOSINE PHOSPHATES

NUCLEIC ACIDS and METALLIC NUCLEATES

NUCLEOTIDES and NUCLEOSIDES

PURINES and PYRIMIDINES

SUGARS and SUGAR PHOSPHATES

GLUTATHIONE COMPOUNDS

SULFHYDRYL REAGENTS

THYMIDINE

COZYMASE

L- and D-AMINO ACIDS, Optically Standardized

RADIOCHEMICALS, Isotopically Labeled with C^{14} , S^{35} or P^{32}

These Schwarz fine chemicals satisfy the exacting requirements of products intended for laboratory and biochemical use.

To assure the user of highest quality and purity, rigid specifications in accordance with latest literature are established for each product, each lot is carefully analyzed and checked before shipment, complete records are permanently kept, and an analysis is furnished the user if desired.

Quantity production resulting from the wide preference and demand for Schwarz high-quality biochemicals provides ample supplies at low cost. Write for informative technical bulletins, specifications, references to literature and latest complete price list.

Visit our Booth #30 At The AAAS Convention

SCHWARZ LABORATORIES, INC.

*Leading Manufacturers of Yeast Biochemicals
and Fine Chemicals*

230B WASHINGTON STREET, MOUNT VERNON, NEW YORK

SL360

VENOMS

AAAS Symposium Volume No. 44

6" x 9", 480 pp., 113 illus.,
index, cloth, Dec. 1956

Price \$9.50. AAAS Members'
cash order price \$8.25

First International Conference on Venoms, with 95 contributors from 18 countries. Comprehensive coverage of all aspects of the problem.

This book covers poisonous fishes and marine organisms, many species of venomous snakes, the Gila monster, toads, scorpions, spiders, caterpillars, wasps and other venom-bearing insects; hyaluronidase-like substances and other spreading factors in venoms; various chemical components of venoms, coagulant and anticoagulant factors, antigenic principles; various experimental and suggested clinical uses of venoms; clinical considerations: mortality rates, treatment of many kinds of envenomation; new developments in serotherapy and types of supplementary medication; dangers of refrigeration for treatment.

Of special interest to: Physicians, pharmacologists, chemists, and zoologists.

AAAS

1515 Mass. Ave., NW, Washington 5, D.C.

STEREOSCOPIC MICROSCOPE for the budget-minded!

Designed and sturdily built for educational or industrial use, UNITRON Model MSL has the same optical and mechanical features found in higher priced instruments.

- Erect, three-dimensional image
- Coated optics and prisms
- Achromatic 2X paired objectives, paired wide field eyepieces
- Working distance 75mm.
- Vertical binocular body with interpupillary and diopter adjustments
- Total focusing excursion 70mm.
- Heavy base, removable glass stage plate, stage clips
- Choice of one magnification 10X, 20X or 30X, extra eyepieces available
- Complete in fitted hardwood cabinet

FREE 10 DAY TRIAL

ALSO AVAILABLE

Model MSL-A with magnifications —
5X or 10X or 15X \$120.00
Extra eyepieces Pair \$19.50
Model LS Stereoscopic Microscope Lamp \$14.75



\$110.00
FOB Boston

UNITRON

INSTRUMENT DIVISION of UNITED SCIENTIFIC CO.
204-206 MILK STREET • BOSTON 9, MASS.

Please rush to me, UNITRON's Microscope Catalog. 4L-2.

Name _____

Company _____

Street _____

City _____ State _____

nearly 80 percent of maximum response. Maximum response occurs at approximately 3300 A, and total range is approximately 1800 to 6000 A. For operation at 1000 v, current amplification is 10^6 , luminous sensitivity is 40 a/lu, and ultraviolet equivalent noise input is 6.6×10^{-16} w. (Radio Corporation of America, Dept. 529)

■ BURETTE permits measurement and delivery of small quantities of liquids heated to temperatures up to 350°F. Heating is done by means of a transparent conductive coating on the outer surface of the graduated tube. Thermal and electrical insulation are provided by a cylindrical glass enclosure. Heating is controlled by a variable transformer. The burette terminates in a 1/4-in. glass-pipe tube fitted with a standard 1/4-in. pipe flange. The two sizes available have capacities of 340 and 820 ml. A fluorescent light extending the full length of the burette provides illumination. (Pressure Products Industries, Inc., Dept. 531)

■ PLASMA JET creates and sustains temperatures greater than 22,000°F. The jet is up to 1/2-in. in diameter and 6-in. long. Systems are available in various power levels ranging from 12.5 to 160 kw. (Giannini Research Laboratories, Dept. 533)

■ SWEEP-FREQUENCY AUDIOMETER operates by fixing the intensity of the test sound and continually varying the signal frequency throughout the test. The level of the acoustic signal in the range 200 to 8000 cy/sec is equivalent to the threshold sensitivity ranges of the average healthy ear. Result of tests are recorded on circular charts. A controlled masking signal generated by a relaxation oscillator is included in the instrument. A bone-conduction receiver is available as an accessory. (Peekel Laboratory of Electronics, Dept. 530)

■ REACTION FLASK for small-scale organic reactions is designed for ease of emptying and cleaning and for interchangeability. Top and bottom sections are separable at a flat flange of 2-in. inside diameter. Standard heating mantles will accommodate all flask sizes. (Kontes Glass Company, Dept. 542)

■ TWO-FLUID PRESSURE TESTER utilizes pure water as the hydraulic fluid entering the unit under test while permitting the use of oil or glycerine in the piston-cylinder chamber. Pressure of 10,000 lb/in.² is generated with force of 17 lb. Capacities range from 200 to 10,000 lb/in.², and accuracy is ± 0.1 percent. (Amthor Testing Instrument Co., Dept. 532)

JOSHUA STERN

National Bureau of Standards

PERSONNEL PLACEMENT

CLASSIFIED: 25¢ per word, minimum charge \$4.25. Use of Box Number counts as 10 additional words. Payment in advance is required.

COPY: For classified ads must reach SCIENCE 2 weeks before date of issue (Friday of every week).

DISPLAY: Rates listed below—no charge for Box number. Monthly invoices will be sent on a charge account basis—provided that satisfactory credit is established.

Single insertion	\$26.00 per inch
13 times in 1 year	24.00 per inch
26 times in 1 year	23.00 per inch
52 times in 1 year	22.00 per inch

For PROOFS on display ads, copy must reach SCIENCE 4 weeks before date of issue (Friday of every week).

Replies to blind ads should be addressed as follows:

Box (give number)
Science
1515 Massachusetts Ave., NW
Washington 5, D.C.

POSITIONS WANTED

Young Scientist; B.A., D.Sc., available 1 July for teaching post in general biology, zoology, parasitology, with or without research. Medical Bureau, Burnside Larson, Director, 900 North Michigan, Chicago. X

POSITIONS OPEN

BACTERIOLOGIST

We have a challenging research position open for a bacteriologist with a B.S. or M.S. degree and some experience in antibiotics. This is an opportunity to use your initiative and creative ability on interesting research projects.

This position offers personal and professional growth as well as liberal benefit program including tuition assistance for graduate study.

Please send résumé to:

E. P. Bloch

ARMOUR RESEARCH FOUNDATION
of Illinois Institute of Technology

10 West 35th Street
Chicago 16, Illinois

POSITIONS WANTED

Endocrine Laboratory operated by M.D. endocrinologist with clinical and research experience desires relocation as unit with medical school, large clinic, or pharmaceutical company. Box 250, SCIENCE. X

Ph.D. Microbiologist, "Big Ten" graduate, now in administrative-research-development with well-known eastern pharmaceutical company, teaching experience, publications. Desires change to greater responsibility and growth in industry as department head or scientific coordination. Will relocate. Box 249, SCIENCE. X

POSITIONS OPEN

Biologist, Histologist, Histochemist, Ph.D. or equivalent. Research institute, New York; to work in the field of experimental diabetes. Starting salary \$7500. Box 248, SCIENCE. 12/12, 19

Chemist-Biochemist: B.S.-M.S. Medical research program. Varied activities: cellular biochemistry, proteins, amino acids, electrolytes. Reply to Medical Research Laboratory, Veterans Administration Hospital, East Orange, N.J. 12/12

(a) **Clinical Microbiologist:** M.D., Ph.D. to supervise bacteriology laboratory, microbiological developmental work, research; laboratory processes 200 bacteriology specimens, 200 syphilis serology specimens daily; large diagnostic clinic, affiliated 500-bed general hospital; midwestern university city. (b) **Biochemist:** recent Ph.D. interested protein isolation; prominent eastern concern; \$7800. (c) **Bacteriologist:** M.S. for newly created position in expanding laboratories, 300-bed general hospital; to \$6600; college city, Southeast. (d) **Biochemist:** Ph.D. capable directing laboratory staff of 35; 400-bed general hospital; new structure to be completed late 1959; California coastal city; \$10,000. Woodward Medical Bureau, Ann Woodward, Director, 185 North Wabash, Chicago. X

Pharmacologist-Physiologist openings in neuropharmacology for persons with some background and interest in this field. B.S., M.S., and Ph.D. levels. Active research programs. Opportunity for advancement. Contact Dr. G. M. Everett, ABBOTT LABORATORIES, North Chicago, Illinois. 11/28; 12/5, 12

SCIENCE TEACHERS, LIBRARIANS, ADMINISTRATORS urgently needed for positions in many states and foreign lands. Monthly no-fee placement journal since 1952 gives complete job data, salaries. Members' qualifications and vacancies listed free. 1 issue, \$1.00. Yearly (12 issues) membership, \$5.00. CRUSADE, SCI. Box 99, Station G, Brooklyn 22, N.Y. ew

FELLOWSHIPS

Division of Radio Physics of the Commonwealth Scientific and Industrial Research Organization, Commonwealth of Australia invites applications for a fellowship in radio astronomy.

The division has its headquarters within the grounds of Sydney University and operates a number of powerful and unique radio telescopes at field stations located in the countryside around Sydney. The appointee will be expected to take part in an active research program in some aspect of radio astronomy.

The fellowship is tenable at Sydney for a period of 2 years. Applicants should have had previous research experience in either radio astronomy or astronomy, and the salary offered will be determined in relation to qualifications and experience, but will be not less than £1400 per annum.

The appointment will be conditional upon a satisfactory medical examination and an initial probationary period of up to 12 months may also be specified.

Fares to Australia, including those of wife and dependent family, will be provided by the organization, and return fares to point of origin will be allowed at the end of the period of appointment in the case of an appointee who is not of Australian nationality.

Applications quoting reference number 780/194 should include full name, place, date and year of birth, nationality, marital state, and present employment, details of academic training, qualifications, research experience, and published work (if any), the names of not more than four persons acquainted with the applicant's academic and professional standing, and the applications should reach the Chief, Division of Radiophysics, C.S.I.R.O., University Grounds, City Road, Chippendale, New South Wales, by 31 December 1958, or the Scientific Attaché, Australian Scientific Liaison Office, 1907 K Street, N.W., Washington 6, D.C. X

The University of British Columbia, Department of Zoology, invites postgraduates to apply for National Research Council postdoctoral fellowships for work in the department's laboratories in Vancouver. Facilities are excellent for experimental and physiological studies of marine and fresh-water fish and invertebrates as well as for field and laboratory studies of birds and mammals, particularly opportunities for field studies of big game animals. Facilities also available in entomology, forest entomology, embryology, and histology. Direct enquiries to Dr. I. M. Cowan, Head, Department of Zoology, or Dr. P. A. Larkin, Director, Institute of Fisheries. X

POSITIONS OPEN

Biologist, Botanist, Zoologist, Ph.D., interested in teaching and research. Contact Jacob Uhrich, Trinity University, San Antonio, Texas. For interviews during AAAS meeting contact me at Shoreham Hotel. X

(a) **Pharmacologist** to direct department, one of leading pharmaceutical companies; staff of 30 to 40 including five M.D.'s and Ph.D.'s; may continue research of own inclination; possibilities of academic connections; Midwest. (b) **Two Ph.D.'s** for supervisory positions including research; one should have broad experience in clinical chemistry, the other would have charge of endocrinology section; **two** scientists should be qualified to direct staffs of 10 to 12; work of both involves methodology; \$8400 to \$12,000; Pacific Coast. (c) **Child Clinical Psychologists:** new position; man preferred; Ph.D. required, community guidance center, large city, Southwest; \$7500. S12-2 Medical Bureau, Burnice Larson, Director, 900 North Michigan, Chicago. X

POSITIONS OPEN

MEDICAL WRITER

Opportunity available for young physician in Professional Service Department of Medical Division. Should have ability and interest in medical writing. Clinical or laboratory experience desirable. Please send complete résumé to:

Technical Employment Coordinator
THE UPJOHN COMPANY
Kalamazoo, Michigan

USE THIS EASY SELF-MAILER to obtain further information

12 December 1958

Readers' Service Information Requisition

It's simple: Mark—Clip—Fold—Mail—No stamp required

This coupon is for your convenience—to facilitate your requests for further information about advertised products and items in Equipment.

From:

Name Position

Company

Street

City Zone State

(Please print or type)

Mark, clip coupon—FOLD HERE along this line—mail

Postage
Will be Paid
by
Addressee

No
Postage Stamp
Necessary
If Mailed in the
United States

BUSINESS REPLY CARD
First Class Permit #12711 New York, N.Y.

Readers' Service

To: **SCIENCE MAGAZINE**
Room 740
11 West 42 Street
New York 36, New York

Fasten Here Only
Staple, Tape, Glue



The Market Place

BOOKS • SERVICES • SUPPLIES • EQUIPMENT

DISPLAY: Rates listed below—no charge for Box number. Monthly invoices will be sent on a charge account basis—provided that satisfactory credit is established.

Single insertion	\$26.00 per inch
13 times in 1 year	24.00 per inch
26 times in 1 year	23.00 per inch
52 times in 1 year	22.00 per inch

For PROOFS on display ads, copy must reach SCIENCE 4 weeks before date of issue (Friday of every week).

SUPPLIES AND EQUIPMENT

LaMotte

Water Soluble pH Indicators

Highly Purified
Instantly Soluble

No mixing — No waiting

Send for LaMotte Catalog

Chemical Controls for:
pH, Chlorine, Phosphates
and Polyphosphates, etc.

LaMotte Chemical Prod. Co.
Dept. H, Chestertown, Md.

SUPPLIES AND EQUIPMENT

albino rats *

*Descendants of the
Sprague-Dawley and
Wistar Strains

Hypophysectomized
Rats

HENRY L. FOSTER, D.V.M.
President and Director
THE CHARLES RIVER BREEDING LABS.
Dept. B, Wilmington, Mass.



Oleic Acid 1-C¹⁴

other High Radiopurity tagged compounds

ISOTOPES SPECIALTIES COMPANY INC.
BOX 688 BURBANK, CALIFORNIA
DIVISION OF NUCLEAR CORPORATION OF AMERICA, INC.

• HYPOPHYSECTOMIZED RATS

Shipped to all points via Air Express
For further information write
HORMONE ASSAY LABORATORIES, Inc.
8159 South Spaulding Ave., Chicago 29, Ill.

F. J. ZEEHANDELAAR Inc.

Wild Animal Importers

286 Clove Road,
New Rochelle, N.Y.

We import specially required
livestock from any part of the
world for research purposes.

TRYPsinized MONKEY KIDNEY
SUSPENSION MONKEY WHOLE
BLOOD — SERUM

Cell suspension packed in wet ice—shipped
via air express—growth guaranteed

WRITE OR WIRE
RESEARCH SUPPLY COMPANY
230 Hillside Avenue — Paramus, N.J.

Sprague-Dawley, Inc.

Pioneers in the development of the
standard laboratory rat.

Sprague-Dawley, Inc.

P.O. Box 2071, Madison 5, Wisconsin
Phone: Cedar 3-5318

TEXAS INBRED MICE COMPANY

Now available: C3H
AKR C57BL
Strong A (C3Hx101)F₁

Mice of all strains derived from pure bred stock
maintained by brother to sister matings and proper
genetic selection.

6140 Alameda, Houston 21, Texas
Phone: JACKSON 9-2764

BOOKS AND MAGAZINES

**Your sets and files of
scientific journals**

are needed by our library and institutional cus-
tomers. Please send us lists and descriptions of
periodical files you are willing to sell at high mar-
ket prices. Write Dept. ASS, CANNER'S, Inc.
Boston 20, Massachusetts

"OUR PREVIOUS AD

created a great deal of interest,
for which we are grateful. Addi-
tional advertising in your magazine
is contemplated."

12 December 1958

Readers' Service

Information Requisition

Use this easy self-mailer to obtain further information about
items or literature from the Equipment section as well as from
advertised products.

EQUIPMENT

Circle below desired number corresponding to:

518	519	522	525	529	530	531
532	533	542				

ADVERTISERS IN THIS ISSUE

In list below, check page number of advertiser from whom you would like
more information. If more than one item appears in ad, letters (A, B, C) are
used to indicate particular items available in order of appearance in advertise-
ment. Where more than one ad appears on page, "U" indicates upper ad, "L"
lower ad, "I" inside ad, "M" middle ad, and "O" outside ad. Advertisements
in Personnel Placement and Market Place are not keyed. A multiplicity of
items is indicated by *. Readers are requested to specify on this coupon the
particular item in which they are interested; otherwise, the request cannot
be processed.

<input type="checkbox"/> 1474	<input type="checkbox"/> 1475*	<input type="checkbox"/> 1478	<input type="checkbox"/> 1480	<input type="checkbox"/> 1518
<input type="checkbox"/> 1519	<input type="checkbox"/> 1520, UO	<input type="checkbox"/> 1520, UI	<input type="checkbox"/> 1520, LO	<input type="checkbox"/> 1520, LI
<input type="checkbox"/> 1521*	<input type="checkbox"/> 1522	<input type="checkbox"/> 1523*	<input type="checkbox"/> 1524, LO	<input type="checkbox"/> 1528

APPLICATION FOR HOTEL RESERVATIONS

125th AAAS MEETING

Washington, D.C., December 26-31, 1958

The list of hotels and their rates and the reservation coupon below are for your convenience in making your hotel room reservation in Washington. Please send your application, *not* to any hotel directly, but to the AAAS Housing Bureau in Washington and thereby avoid delay and confusion. The experienced Housing Bureau will make assignments promptly; a confirmation will be sent you in two weeks or less.

As in any city, single-bedded rooms at minimum rates may become scarce; double rooms for single occupancy cost more; for a lower rate, share a twin-bedded room with a colleague. Most hotels will place comfortable rollaway beds in rooms or suites at \$2.00 to \$2.50 per night. Mail your application *now* to secure your first choice of desired accommodations. All requests for reservations must give a definite date and estimated hour of arrival, and also probable date of departure.

AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE

Rates for Rooms with Bath

Hotels with an asterisk have sessions in their public rooms. For a list of headquarters of each participating society and section, see page 151, *Science*, July 18.

Hotel	Single	Double Bed	Twin Bed	Suite
*Dupont Plaza	\$10.00-11.00	\$13.00-14.00	\$13.00-14.00	\$21.00-27.00
*Sheraton-Park	8.00-12.00	12.00-14.50	11.00-16.00	20.00-60.00
*Shoreham	all 9.00	all 12.00	all 12.00	20.00-50.00
*Statler	all 10.00	all 14.00	all 14.00	24.00-30.00
*Washington	7.00- 8.00	11.00-12.50	11.00-12.50	24.50-45.00
*Willard	10.00-12.50	13.00-17.00	14.00-18.00	25.00-35.00
Roosevelt	7.00- 9.00		10.00-12.00	18.00-24.00
Sheraton-Carlton	12.00-17.00		17.00-21.00	
Windsor Park	all 9.00	all 14.00	all 14.00	13.00-18.00

----- THIS IS YOUR HOUSING RESERVATION COUPON -----

AAAS Housing Bureau
1616 K Street, N.W.
Washington 6, D.C.

Date of Application

Please reserve the following accommodations for the 125th Meeting of the AAAS in Washington, D.C., Dec. 26-31, 1958:

TYPE OF ACCOMMODATION DESIRED

Single Room Desired Rate Maximum Rate
Double-Bedded Room Desired Rate Maximum Rate Number in party
Twin-Bedded Room Desired Rate Maximum Rate
Suite Desired Rate Maximum Rate Sharing this room will be:
(Attach list if this space is insufficient. The name and address of each person, including yourself, must be listed.)

First Choice Hotel Second Choice Hotel Third Choice Hotel

DATE OF ARRIVAL DEPARTURE DATE
(These must be indicated—add approximate hour, a.m. or p.m.)

NAME
(Individual requesting reservation) (Please print or type)

ADDRESS
(Street) (City and Zone) (State)

Mail this now to the Housing Bureau. Rooms will be assigned and confirmed in order of receipt of reservation.

NOW ACTIVELY AIDING ACADEMIC TRAINING IN NUCLEONICS



Student Reactor Training Laboratory. Instructor inserts neutron-sensitive scintillation detector into automatic traversing mechanism while students utilize specialized instrumentation for neutron flux measurements, and gamma, beta, and alpha sample analysis.

• first nuclear-chicago reactor training laboratories now delivered to colleges and universities

- Deliveries have been completed to these institutions:

California Institute of Technology

University of Connecticut

State University of Iowa

University of Nevada

Occidental College

University of Rochester

Texas Technological College

Utah State University

Nuclear-Chicago's Sub-critical Reactor Laboratory, first announced in January 1958, has been installed at eight leading U.S. Colleges and Universities. Designed for student training, the complete laboratory consists of the new Model 9000 Student Sub-critical Reactor, a carefully selected group of radiation detection and recording instruments, and a manual of experiments specially prepared for the Student Reactor and related nuclear counting systems. Instrumentation and experiments are designed to familiarize students with basic nuclear detecting and measuring devices and analytical methods, and to provide valuable reactor training in determinations of neutron flux, Fermi Age in water, relaxation lengths, multiplication factors, neutron activation, and other reactor properties. If you have not yet considered this unique package training program for your institution ask us to send our representative to explain it in detail.

Fine Instruments - Research Quality Radiochemicals



nuclear-chicago
CORPORATION
237 WEST ERIE STREET • CHICAGO 10, ILLINOIS

CS

scin-
rsing
cial-
flux
and

ties

d in
Uni-
sists
cted
nual
ated
gned
rices
g in
yths,
ties.
n for
etail.

70

~
INOIS